The Relationship between Infantile Postural Asymmetry and unsettled behavior in babies: A quantitative observational study

Julie Ellwood

THE RELATIONSHIP BETWEEN INFANTILE POSTURAL ASYMMETRY AND UNSETTLED BEHAVIOUR IN BABIES: A QUANTITATIVE OBSERVATIONAL STUDY

J. A. ELLWOOD

Professional Doctorate

2016

UNIVERSITY OF BEDFORDSHIRE

THE RELATIONSHIP BETWEEN INFANTILE POSTURAL ASYMMETRY AND UNSETTLED BEHAVIOUR IN BABIES: A QUANTITATIVE OBSERVATIONAL STUDY

by

J.A. ELLWOOD

A thesis submitted to the University of Bedfordshire in partial fulfilment of the requirements for the degree of Professional Doctorate

UNIVERSITY OF BEDFORDSHIRE

Institute for Health Research

January 2016

For all mothers, especially my own.

Abstract

Background: Unsettled infant behaviour is a common problem of infancy without known aetiology or effective management, and it is costly in both social and economic terms. Some osteopaths propose that musculoskeletal dysfunction contributes to unsettled infant behaviour, yet reported improvement following osteopathic treatment is anecdotal. A primary issue is the absence of a measurement tool to test musculoskeletal dysfunction in infants.

Aims and Objectives: This research aimed to investigate: the reliability and validity of the infantile postural asymmetry (IPA) measurement scale; whether there was a relationship between IPA and unsettled infant behaviour as measured by the Revised Infant Behavior Questionnaire – short form (IBQ-Rs); and whether any relationship between IPA and unsettled infant behaviour was mediated by, or confounded with, the demographic variables of age, sex, birth weight and weight gain in twelve- to sixteen-week-old infants.

Methods: Fifty-eight infants aged twelve- to sixteen-weeks-old were recruited through public health clinics, and their behaviour was assessed using the parent-report IBQ-Rs. Infantile asymmetry was measured using observer ratings of spontaneous movements in the IPA scale. A quantitative cross-sectional observational design was used to investigate the relationship between IPA and unsettled behaviour.

Results: An association between unsettled behaviour and musculoskeletal dysfunction was not found in twelve- to sixteen-week-old infants using the IPA measurement scale. Ratings for the trunk convexity parameter of the IPA scale were unreliable and excluded from statistical analysis. A significant difference between high and low cervical rotation deficit groups for Surgency was detected in female babies and needs further examination. Some subsets of the IBQ-Rs were unstable when measuring behaviour in twelve- to sixteen-week-old infants. Future research targeting infants younger than twelve-weeks-old, and presenting with unsettled behaviour, is indicated.

Conclusion: A causal relationship between unsettled infant behaviour and musculoskeletal dysfunction is still unproven. The literature suggests benefits associated with a consistent approach to providing parents with information, support and advice on normal behaviour patterns and optimal handling of infants. Non-specific effects cannot be ruled out in reported improvements following osteopathic treatment. Management strategies require early implementation and a multidisciplinary approach. The absence of common terminology in infant behaviour problems is an obstacle in cross-professional communication. A role for osteopathy may be in developing a shared language to facilitate management and research, and to examine the importance of positioning and handling practices on infant asymmetry and the relationship with the musculoskeletal system.

Acknowledgements

I would like to express my deepest gratitude to my supervisors, Dr Michael Ford and Professor Alf Nicholson, for their invaluable time, advice and guidance in doing this research. I could not have imagined having better supervisors for my Professional Doctorate study.

Besides my supervisors, I would like to thank my tutors at the British School of Osteopathy (BSO); Professor Stephen Tyreman, Steve Vogel and Dr Jorge Esteves, for their encouragement, support, insightful comments, and hard questions. A special thanks also to Will Podmore, who was so tolerant of my relentless requests from the BSO library.

I wish to acknowledge my Professional Doctorate colleagues, Cindy, Jerry and Hil, partners in study and friends for life. I would also like to thank my good friend Eve Mac Searraigh for taking time out from her busy schedule to serve as my external reader.

A very special thanks goes out to the public health nurses who so willingly invited me into their spaces of work, so that the practical element of this research could be conducted. In particular, I would like to thank Fiola Murphy, Martina O Dowd and Maire Mc Gettrick for their commitment to this study.

To all the parents who gave their time to take part in this study and openly shared their experiences with me, without which this research would not have been possible.

To my parents, brother and sisters, for all their love and encouragement. I feel so lucky. To the four young jewels in my life, Mackenzie, Scarlett, Kiefer and Mathilde, for their welcome distractions throughout the last few years, that were so important in keeping me grounded. Finally, to my loving husband Patrick, who cheered me up with endless cups of coffee and warm jokes, and who made the demands of this research on our family so tolerable. There are no words.

Declaration

I declare that this thesis is my own unaided work. It is being submitted for the degree of Professional Doctorate at the University of Bedfordshire. It has not been submitted before for any degree or examination in any other University.

Name of candidate: Julie Ellwood

Signature:

Date:

List of Contents

List of Tables

List of Figures

List of Abbreviations

ADBB - Alarm Distress Baby Scale

ADHD - Attention deficit hyperactivity disorder

CAM – Complementary and Alternative Medicine

CI - Confidence Interval

CMPA/CMPI - Cows' milk protein allergy/intolerance

CMT – Congenital muscular torticollis

CPQ - Crying Patterns Questionnaire

CRB - Criminal Records Bureau

CRD - Cervical rotation deficit

DDH - Developmental dysplasia of the hip

DP – Deformational plagiocephaly

ECBQ - Early Childhood Behaviour Questionnaire

EITQ - Early Infant Temperament Questionnaire

GORD - Gastro-oesophageal reflux disease

GOsC - General Osteopathic Council

IBQ – Infant Behavior Questionnaire

IBQ-R – Revised Infant Behavior Questionnaire

IBQ-Rs – Revised Infant Behavior Questionnaire – short form

ICC - Intraclass correlation coefficients

IPA – Infantile Postural Asymmetry

ITSC - Infant-Toddler Symptom Checklist

LOS - Length of stay in hospital

NBAS - Neonatal Behavioral Assessment Scale

NCOR - National Council for Osteopathic Research

NEG - Negative Affectivity (negative emotional reactivity)

NICU - Neonatal intensive care unit

NYLS - New York Longitudinal Study

OCF – Osteopathy in the cranial field

OMT – Osteopathic manipulative therapy

PHC – Public health clinic

PHN – Public health nurse

PIS - Parent Information Sheet

PRM - Primary respiratory mechanism

RCT – Randomised controlled trial

REG - Orienting/Regulation (self-regulatory mechanisms of attention)

RITQ - Revised Infant Temperament Questionnaire

SCM - Sternocleidomastoid muscle

SDSS - Somatic dysfunction severity score

SIDS - Sudden infant death syndrome

SSRD - Single system research designs

SUR – Surgency/Extraversion (positive emotional reactivity)

TC - Trunk Convexity

TMBT - Transient mechanical birth trauma

Chapter 1 – Introduction

This thesis is motivated by the idea that musculoskeletal dysfunction could be a contributing factor in infants who display symptoms of unsettled behaviour. Were it possible to measure musculoskeletal dysfunction in a standardised way, an association with unsettled infant behaviour could be investigated and the scope of osteopathic treatment could be developed. This introductory chapter will outline the background to the research study. It will highlight gaps in current knowledge and the new knowledge being sought by linking together the four concepts of unsettled infant behaviour, infant temperament measurement, osteopathic examination of the musculoskeletal system in infants and infantile postural asymmetry, to demonstrate how the research hypothesis was reached. A brief overview of the subsequent chapters is provided in which the aforementioned themes are elaborated upon, guiding the reader through the sequence of information that will arise throughout the thesis. Finally the aims of this study are discussed, followed by the rationale considered to arrive at these aims and to the specific research topic.

1.1 Background of study

Unsettled infant behaviour is among the most common difficulties reported by parents in the first few months of a baby's life (Wake *et al,* 2006). The prevalence of unsettled infant behaviour, which to date is predominantly reported in developed countries, varies from eleven percent (St James-Roberts & Halil, 1991) to thirty-five percent (Carmichael & Williams, 1983). The prevalence estimates are affected by the variation of different crying patterns, in different infants and at different ages, which is associated with the phenomenon of unsettled behaviour and persistent crying (St James-Roberts & Halil, 1991). High levels of multiple health service usage are required (McCallum *et al,* 2011) at a significant cost to Health Service budgets (Morris *et al,* 2001). In Australia, GP visits were found to be, on average, 7.7 times higher than normal in the first six months postpartum (Gunn *et al*, 1996). One of the main issues is that there is a lack of consensus among health professionals, and care givers, about the nature and cause of the unsettled behaviour and how to manage it.

Some osteopaths have proposed a relationship between unsettled infant behaviour and musculoskeletal dysfunction and recommend osteopathic treatment (Lim, 2006; Philippi *et al*, 2006a; Pizzolorusso *et al*, 2011). Osteopathic treatment has been claimed to have a positive effect on unsettled infant behaviour yet this reported improvement is purely anecdotal (Lim, 2006). The ability to apply a standardised measurement of musculoskeletal dysfunction in infants would improve the potential to measure the effects of osteopathic treatment. This, in turn, could be used in the testing of osteopathic approaches on unsettled infant behaviour.

The Infantile Postural Asymmetry (IPA) measurement scale was described by Philippi and colleagues in 2004. This scale measures the coincidence of cervical spine rotation deficit (reduced rotation of the neck) and trunk convexity (curvature of the back). These two parameters have been associated with musculoskeletal dysfunction in infants (Miller *et al*, 2013) and were identified by Philippi *et al* (2004) to be reproducible when measured by different osteopathic practitioners. In addition, Philippi *et al* (2006a) demonstrated a significant improvement on the IPA scale following osteopathic treatment. The validity of the IPA measurement scale has not been fully evaluated. Existing work is limited by being carried out by one group of researchers; it has not been tested against the current gold standard, radiography, and therefore needs further exploration. Yet it is the first time a non-invasive measurement scale has been developed to identify levels of infantile asymmetry, which could be a valuable tool for future research.

Of particular interest in this thesis is whether a relationship between the IPA measurement scale and unsettled infant behaviour can be detected, as this may suggest that the musculoskeletal factors are involved in part of the presentation of unsettled infant behaviour. If the reported improvement in IPA that Philippi *et al* (2006a) demonstrated with osteopathic treatment can be verified and reproduced, this would provide some proof of the concept that osteopathy can be beneficial in the treatment of IPA, and perhaps also unsettled infant behaviour. It would provide a measurement method to ascertain one outcome domain and be a foundation for use in a randomised controlled trial, which would evaluate effectiveness of treatments.

Within the scope of this thesis there are two key gaps in current knowledge. Firstly, it is not known if the IPA scale is a reliable tool for measuring musculoskeletal dysfunction in infants. Secondly, a relationship between musculoskeletal dysfunction and unsettled behaviour in infants has not been established. If the IPA scale is found to be an accurate and reliable method of measuring musculoskeletal dysfunction in infants, it may be possible to use this measurement to investigate a link between musculoskeletal dysfunction and unsettled infant behaviour. To summarise, this study might elucidate one possible causal factor in unsettled infant behaviour together with a method of assessing this factor and thereby offering the assessment of potential treatment options.

1.2 Reviewing the chapters

The first ten chapters of this thesis aim to examine four core themes running through the research. Current knowledge of unsettled infant behaviour will be examined, with particular emphasis on addressing the inconsistencies in terminology, proposed causes, presentation of symptoms and long-term effects. External factors, which may contribute to infant unsettledness will be explored together with support and management protocols. The concept of infant temperament measurement for behaviour studies will be introduced, as well as how measurement systems have developed with growing knowledge on how best to capture the important aspects of behaviour. The osteopathic perspective on what causes infant distress and how to treat it will be outlined and critically appraised. This will lead onto the osteopathic interest in the musculoskeletal systems of unsettled infants, how this relates to the subject of asymmetry and the potential role of the infantile postural asymmetry measurement scale will be introduced.

Unsettled infant behaviour is the first of four core themes addressed in this thesis. This is a large complex topic area and is, therefore, divided over five chapters (chapters 2-6). Unsettled infant behaviour is introduced in chapter 2. Terms associated with unsettled infant behaviour are described, such as problematic crying and colic. The importance of understanding normal crying behaviours and being able to differentiate these from problematic crying is outlined. Reported prevalence ratings and cost implications are presented, along with how these are affected by poorly defined and inconsistently used terminology.

Chapter 3 continues with the theme of unsettled infant behaviour and examines a number of the more commonly proposed aetiologies including reflux, cows' milk protein allergy, lactose intolerance and gut irritability. There is emphasis on the challenge of deciphering the presenting symptomology of infantile complaints due to an overlap of many of the symptoms. The impact this has on making a definitive diagnosis and management plan, which is the cause of much confusion and frustration for both parents and clinicians, is also discussed.

Regulatory problems in infancy are considered in chapter 4 and the proposed influence on unsettled infant behaviour. The inter-relationship between different regulatory problems, in particular sleep dysregulation and feeding difficulties, is examined. There are different views on how regulatory problems interact with unsettled infant behaviour demonstrating the confusion and disagreement surrounding this topic, with some suggesting a direct causal relationship (Papoušek & von Hofacker, 1998; White *et al*, 2000) whereas others propose they are separate pathologies (St James-Roberts & Peachey, 2011). Although much is still not understood about the processes that underlie infant dysregulation, the use of behavioural intervention programmes for parents appears to promote a positive parent–child relationship and provide the most consistent influence on behavioural development.

The role of the mother-infant dyad in unsettled behaviour, offering some insights into the complexity of this subject, is presented in chapter 5. Behaviour and health in pregnancy and whether the management of the birth process influences behaviour outcomes of the infant is discussed. Addressed also are the potential effects of post-partum behaviour such as maternal mood, different care-giving practices and baby handling. Chapter 5 concludes by noting that although much of the literature suggests a causal role of maternal mood on infant behaviour, the direction of effect appears to be reciprocal. Providing information for parents on normal infant crying patterns and effectively reading baby cues is shown to be effective.

Risk factors associated with the mismanagement of unsettled infant behaviour are presented in chapter 6. The relationship between child abuse and unsettled infant behaviour is outlined with the observation that irritability and crying are the primary aggravating factors in infants who have had repetitive and violent shaking (Ludwig, 1984; Singer & Rosenberg, 1992). This section on unsettled infant behaviour concludes with the practicalities of managing unsettled behaviour through diet, medication and infant handling, and outlines why it persists in being a misunderstood phenomenon of infancy.

The measurement of infant temperament is the second core theme of this thesis and is introduced in chapter 7. This chapter starts by explaining the concept of infant temperament and how it determines infant behaviour. Similar to the mother-infant dyad discussed in chapter 5, the effects of parental perceptions on infant temperament is discussed. There is an exploration into the history of measuring infant temperament, differences in methods, the associated strengths and weaknesses, and improvements made in recent developments of infant temperament measurement. This chapter concludes with looking at specific difficulties of stability when choosing a temperament assessment tool for early infancy.

Rothbart's Infant Behavior Questionnaire (IBQ), a parent-report questionnaire for infant temperament measurement, is introduced in chapter 8. The reasons for selecting Rothbart's IBQ's for further examination with regard to examining behaviour in early infancy is outlined. Developments in revised versions of the IBQ and validation of shorter forms for use in a variety of research environments are of particular interest in this thesis. Chapter 8 concludes with discussing which questionnaire was chosen for the current study and justifications for the decisions made, with reference to the psychometric properties of the questionnaire and the research question for this thesis.

The osteopathic perspective on infant behaviour and its relationship with the musculoskeletal system is the third core theme explored in this thesis and will be discussed in chapter 9. Osteopathy in the cranial field will be critically appraised, with emphasis on the paucity of research in this field and the impact of this on osteopathic practice. Birth trauma is reviewed, along with the effects that many osteopaths believe this has on the musculoskeletal system of newborns. The osteopathic approach to treatment of infant disorders and evidence for its effectiveness is evaluated, which highlights the need for standardised measurement systems by which osteopathic practice can be assessed and compared with other treatment modalities.

Asymmetry in infancy and how this relates, from an osteopathic perspective, to musculoskeletal dysfunction is the fourth and final core theme and is introduced in Chapter 10. The history of the identification of asymmetry as pathology in infants is presented. Development of terminology and categorising asymmetries depending on the prominent features is also addressed. Asymmetries most often associated with infancy are discussed, such as craniosynostosis, deformational plagiocephaly, torticollis and positional preference. Similarities in the symptom patterns of these conditions is noted and the contribution this makes to difficulties with classification of asymmetry. The significance of sleep position is debated, and how the 'back to sleep' campaign has impacted on the physical development of infants. The need for early detection, monitoring and management of infants with asymmetrical patterns highlights the limitations of current measurement methods of asymmetry due to risks of recurrent use of radiography and the need for a non-invasive alternative.

The term Infantile Postural Asymmetry (IPA), coined by Philippi *et al* (2006a), is also introduced in chapter 10. The idea of Infantile Postural Asymmetry as a descriptor for asymmetrical posture observed in some babies during osteopathic assessments is suggested, where previously, the most prominent feature of asymmetry would be reported. The IPA measurement scale is described together with the potential advances in diagnosing, monitoring and managing asymmetry, should it prove to be a reliable measurement tool.

The objective of this thesis is to link the four core themes of 1) unsettled infant behaviour 2) how temperament is measured in infants, 3) an osteopathic approach to unsettled infant behaviour and the association, if any, with musculoskeletal dysfunction and 4) infantile postural asymmetry and the utility of a standardised measurement of the musculoskeletal system in infants by using the IPA scale. Together these form the research topic "The relationship between Infantile Postural Asymmetry and unsettled behaviour in babies: a quantitative observational study". The ability to measure musculoskeletal dysfunction by using Philippi's IPA scale, which has also shown a role for osteopathy in treating IPA (Philippi *et al*, 2006a), and to demonstrate a potential link with unsettled infant behaviour opens up an opportunity for further research and developments in the field of paediatric osteopathy (Philippi *et al*, 2004; Philippi *et al*, 2006b). To date, the research into IPA relies mostly on a single research group (Philippi *et al,* 2004; Philippi *et al,* 2006a; Philippi *et al,* 2006b) leaving potential for bias in the findings. Although radiography is the current gold standard for diagnosing and managing infantile asymmetries, particularly in circumstances where non-resolving asymmetry is suspected, there are limitations in measuring this against the IPA methodology due to the risk of unnecessary overexposure to radiation.

The methods used in this study including design, participants, materials, measures, equipment, procedures and ethics are described in chapter 11, followed by data analysis and results in chapter 12. The thesis concludes with a discussion of the results and how these relate to the literature. There is analysis of what new information this has brought to the topics of interest, in particular, unsettled behaviour in infants, the possible contribution of musculoskeletal dysfunction and the role of paediatric osteopathy. The limitations of this study are discussed and there are suggestions for how the findings of the study might be further developed in future research.

1.3 Aims of study and rationale

Osteopathic treatment of the musculoskeletal system to relieve the symptoms of discomfort and help to resolve unsettled infant behaviour is poorly researched and evidence of effectiveness is anecdotal. A primary issue is the absence of a specific diagnostic tool to test the hypothesis that disturbance of the musculoskeletal system may contribute to unsettled infant behaviour. With this in mind, the aims of the current research study are:

a) to investigate the reliability and validity of the Philippi *et al* (2004) IPA measurement scale for measuring infantile postural asymmetry,

b) to establish whether there is a relationship between IPA and unsettled behaviour in twelve- to sixteen-week-old infants, as measured by the Revised Infant Behavior Questionnaire – short form (IBQ-Rs) (Putnam *et al*, 2014) and

c) to investigate whether any relationship between IPA and unsettled behaviour is mediated by, or confounded with, the demographic and developmental variables of age, gender, weight and weight gain in twelve- to sixteen-week-old infants.

If an association is found between IPA and unsettled infant behaviour, and osteopathic treatment improves IPA (Philippi *et al*, 2006a) this would support the utility of testing osteopathic treatments for unsettled infant behaviour.

These aims are based on the rationale that, when investigating infants who present with symptoms of unsettled behaviour, there is a benefit in examining the musculoskeletal system for signs of dysfunction. If musculoskeletal dysfunction can be measured by using the IPA scale then it may be possible to find if a relationship exists between IPA and unsettled behaviour in infants, as measured by the IBQ-Rs. Finding a relationship could lead to future potential of the IPA scale for monitoring the progression or resolution of symptomatic infants where the musculoskeletal dysfunction shows a causal relationship with unsettled behaviour. Therefore the title of this study is:

The relationship between Infantile Postural Asymmetry and unsettled behaviour in babies: a quantitative observational study.

1.4 Chapter summary

Identifying a definitive cause for unsettled behaviour in infants has been a source of much examination and research. Many different hypotheses have been suggested yet much is still unknown. From an osteopathic perspective of particular interest, when presented with an infant who has a history of persistent unsettledness, is whether there are components of the musculoskeletal system causing discomfort and, therefore, distress in that infant. There is a paucity of research in the entire spectrum of osteopathic application and, therefore, many gaps in the current knowledge. In order to develop the scope of osteopathy in paediatric care, it is important to approach research topics in a logical manner and first identify some fundamental facts. For example, before investigating whether osteopathic treatment is useful in the treatment of any condition, a standardised and reliable method of measurement is required.

To this end, the current research examines the validity of the IPA measurement scale for diagnosing IPA and then investigates the utility of this scale in finding an association between unsettled infant behaviour and IPA, which would indicate musculoskeletal dysfunction as a contributing factor to unsettled infant behaviour. The results of this research will be threefold in generating new and valuable knowledge about whether infantile asymmetry is associated with musculoskeletal dysfunction, if the IPA scale can be used for detecting IPA and also musculoskeletal dysfunction, and finally if musculoskeletal dysfunction plays a role in causing infants to be unsettled in the first months of life. Finding these answers opens up the potential of osteopathic practice for treating paediatric unsettledness, and regardless of the outcome, it will assist in directing future research in the field, not only of osteopathy but also of unsettled infant behaviour.

<u>Chapter 2 – Common terms for unsettled infant behaviour</u>

Unsettled infant behaviour is a term commonly used to describe a range of behaviours in babies aged up to twelve months, which include prolonged episodes of crying, inconsolable crying, resistance to soothing, sleeping difficulties and/or feeding problems (Don *et al*, 2002). Descriptions of unsettled behaviour vary depending on the parent, the medical practitioner and the researcher (Douglas *et al*, 2012). One of the issues with drawing information from this wide subject is the variations in terms used and definitions associated with those terms, which can be inconsistent and confusing (Gormally & Barr, 1997). Terms most commonly associated with unsettled infant behaviour include problematic crying, prolonged or excessive crying and infantile colic. In this document, the term ‘unsettled infant behaviour’ will be used by the researcher but when referencing other publications and writings, the original terminology used by the author will be maintained.

Because of the scale of this subject, the next five chapters will be dedicated to examining unsettled infant behaviour from different perspectives. This chapter introduces the topic and the impact it has on the healthcare system. This chapter also describes the two other terms most associated with unsettled infant behaviour, i.e. problematic crying and infantile colic, and compares these with normal crying patterns in infants. In chapter 3, the possible causes of unsettled behaviour; e.g. gastro-oesophageal reflux disease (GORD) or ‘reflux’, cow’s milk protein allergy (CMPA), lactose intolerance and gut irritability, are described along with the difficulty with accurate diagnosis and limitations of many treatment protocols. The relationship between unsettled infant behaviour and regulatory problems such as feeding and sleeping is addressed in chapter 4. Chapter 5 looks at the interactions between parents and their babies and how the mother-infant dyad affects infant behaviour and vice versa. The importance of providing support for parents is emphasised also in chapter 5. Finally chapter 6 concludes the discussion on unsettled infant behaviour by addressing the long-term effects and risk factors associated with inadequate management. This leads into the next section of this thesis, in chapter 7, infant temperament and associated measurement methods.

2.1 Impact of unsettled infant behaviour

Unsettled infant behaviour is a significant problem, which is predominantly researched in high income developed societies (Carmichael & Williams, 1983; Goldfeld *et al*, 2003; Hort, 1992; St James-Roberts & Halil, 1991; Thomas, 1981) and among educated mothers (Don *et al*, 2002; Goldfeld *et al*, 2003; Hort, 1992; McCallum *et al*, 2011), with limited research from low income countries (Fisher *et al*, 2011). Additionally, most research has been on clinical samples, so little is known about crying in infants whose parents have not sought professional help (St James-Roberts & Halil, 1991). A variety of factors can influence estimates of the prevalence of unsettled infant behaviour, such as how the behaviour is defined, the age of the infant and the methodology used. The rate of unsettled infant behaviour has been reported to be as high as thirty-five percent (Hogdall *et al*, 1991). However reports suggest a prevalence of twenty to twenty-five percent of all infants show symptoms of excessive crying, sleeping difficulties and/or feeding problems in the first year of life (Fisher *et al,* 2011; Hemmi *et al*, 2011; Hiscock & Jordan, 2004; Hort, 1992) indicating that unsettled infant behaviour has a considerable impact on many family situations.

The practice of baby carrying to settle babies is widely used, but the time spent doing this varies across different cultures and there are conflicting reports about the effectiveness of this practice on infant crying time. St James-Roberts *et al* (2006) propose crying, fussiness and irritability are present in infants of all cultures. In a comparative study using validated behaviour diaries, investigating methods of parenting and associated infant crying and sleeping in three very different care-giving societies, it was found that although infants who were carried less cried more at two and five weeks of age, the groups did not differ in number of inconsolable bouts or in colicky crying at five weeks of age (St James-Roberts *et al*, 2006). However, other studies report the absolute amount of crying varies significantly between cultures (Barr, 1990; Barr *et al*, 1991a; Goldberg, 1972). Hunziker and Barr (1986) found in a randomised controlled trial that increased holding and carrying by parents reduced infant crying at five to six weeks of age, though the study is limited by not being blinded. Wolff makes the observation that psychologically significant interventions such as human voice and figures (compared to non-human distraction) became increasingly important and effective soothing interventions after the second week of life (Wolff, 1969 as cited in Hunziker & Barr, 1986). These findings were not confirmed in two subsequent studies (St James-Roberts *et al*, 1995; Walker & Menaheim, 1994) and increased carrying was not found to be an effective treatment when infants were already crying a lot (Barr *et al*, 1991b). Different care-giving practices and the impact on infant behaviour is discussed in more detail in chapter 5. While acknowledging the limitations of research in terms of diverse cultural practices, the evidence that is available supports the argument that unsettled infant behaviour is not a problem exclusive to western developed societies.

Increased demands placed on post-natal support services and health providers due to the lack the preparedness for motherhood is widely reported (George, 2005; McVeigh, 1997; Nelson, 2003). High levels of multiple health service use have been found in the post-partum period, including visits to emergency departments (Don *et al*, 2002; Hort, 1992; McCallum *et al*, 2011). In a large-scale retrospective survey using health insurance records, Gunn *et al* (1996) found that mothers and their infants visited their GP 7.7 times more than normal in the first four months post-partum and used 2.8 different health services. Similarly, Armstrong *et al* (2000) found fifty-seven percent of new mothers had sought advice from three or more different health professionals. The large retrospective study of Hort (1992) found that, despite high usage of a variety of health service providers, up to one quarter of mothers did not find any service helpful. As the potential for recall bias is a limitation of cross-sectional surveys and diaries, Goldfeld *et al* (2003) conducted a prospective cohort study where primary data was collected from parentally filled questionnaires. They found a significant proportion of visits to healthcare providers in the first twelve months were related to problems with feeding, sleeping and unsettled behaviour (Goldfeld *et al*, 2003). This study was limited by being an unrepresentative socio-demographic population of educated first time parents, who have potentially different health service utilisation rates from those with more than one child, and who represent only forty percent of annual births. In a recent report, McCallum *et al (2011)* proposed that the need for assistance in managing unsettled infant behaviour was still not appreciated, even though most evidence suggests a significant increase on demands across all healthcare providers during the first twelve months, indicative of the support required by mothers and their infants.

There is a substantial cost implication to the health service caused by inconsistency in advice, contradictory information and confusion of parents (Fisher *et al*, 2011). A cost burden analysis found that the annual cost to the UK National Health Service of infant crying and sleeping problems in the first twelve weeks of life was £65 million (Morris *et al*, 2001). In a prospective randomised controlled trial of 610 mothers, Morris *et al* (2001) found that the introduction of an infant behavioural programme provided a small but significant improvement to unsettled behaviour at a small cost. However the distribution of educational leaflets to parents on management of infant behaviour was of no cost benefit. From qualitative research looking at attitudes and supports for parents of unsettled babies, Douglas *et al* (2012) concluded that the development of education resources, best practice guidelines and shared assessment frameworks for Primary Care Practitioners and the improvement of strategies for cross-professional communication, are required to enhance the health outcomes and decrease the burden on services of this complex post-birth problem. While generalisation from qualitative research is not possible, it is consistent with evidence demonstrating the benefits of cross-professional collaboration in maternity care (Martin & Kasperski, 2010). Don *et al* (2002) demonstrated that an integrated and individualised multidisciplinary residential programme is an effective management tool for unsettled infants. This study is weakened by a high drop-out rate and lack of a control group, but the over-riding consensus suggests that implementing a consistent multidisciplinary approach to managing unsettled infant behaviour would alleviate much of the distress for new mothers so that feelings of guilt, helplessness and desperation can be avoided, and would help to control demands on health service usage (Fisher *et al*, 2011).

Unsettledness and crying can be the presenting symptoms in almost any pathological condition of infancy (O'Neill *et al*, 2014 p.95). In trying to address the unsettled behaviour, there is a risk of incorrectly diagnosing conditions such as lactose intolerance, food allergies and reflux (Don *et al*, 2002; Douglas & Hiscock, 2010). Clinicians who struggle to find the best way to approach and manage these infants are not helped by the paucity of high quality research (Oberklaid, 2000). Substantial research has been conducted to investigate mechanisms underlying unsettled infant behaviour, yet much of it is methodologically limited with cross-sectional designs and small or unrepresentative samples predominating. Among the experimental intervention studies, many have methodological problems such as selection bias and absence of blinding, and are further confounded by the natural spontaneous resolution of unsettled infant behaviour (Oberklaid 2000). Armstrong *et al* (2000) found that infant behaviour management was the primary difficulty identified following assessment and short-term focused intervention of unsettled infants in a residential setting. The majority of the children had previously been diagnosed with one or more medical conditions, most commonly, reflux and ninety-five percent had been put on medication. All medications were ceased on admission and the intervention focused on educating the mothers on normal developmental changes in infants combined with modification of mother-infant interactions, feeding and sleeping patterns. Although this study was limited by having a small sample (n=51), this suggests a possible high prevalence of pathologising normal infant behaviour (Armstrong *et al*, 2000). When an infant is presenting with unsettled behaviour, the main difficulty is establishing if the unsettledness is caused by a treatable condition. In most infantile conditions, the prominent complaint is problematic crying and incorrect management of such infants' risks exacerbating their symptoms (Armstrong *et al*, 2000).

2.2 Problematic crying

Although problematic crying is a prominent feature of unsettled infant behaviour, crying is also part of normal developmental processes in infancy rather than a distinct clinical condition (Armstrong *et al*, 2000; Hiscock & Jordan, 2004; St

James-Roberts *et al*, 1998); it is an infant's method of communicating hunger, tiredness or discomfort. Understanding normal infant crying patterns is important to determine how this differs from problematic crying (Barr, 1990a; Barr *et al*, 1991; Hunziker & Barr, 1986) and the mechanisms of behavioural development involved (Barr, 1998).

Brazelton's (1962) early work in which eighty mothers documented their infants' crying in a diary for twelve weeks demonstrated a normal crying peak at six weeks in the majority of infants. Normal daily crying patterns tend to increase in the first few weeks to approximately two hours a day. This increases to a peak of three hours a day in the second month but normally will decrease by the fourth month (Barr *et al*, 1988, Barr *et al*, 1989; Brazelton, 1962; Hill *et al*, 1992; Hiscock & Jordan, 2004). Evidence of this early crying peak has been found cross-culturally, suggesting that it is a universal feature of infancy (Barr *et al*, 1991a; St James-Roberts *et al*, 1998). Barr *et al* (1991a) demonstrated in forty-six !Kung San infants from the hunter-gatherer society in north-western Botswana that, despite markedly different caretaking practices predisposing to quieter infants, crying and fretting were significantly greater during the first three months, and a peak pattern was present. During the first six months, episodes of crying tend to cluster in the evening, but can occur throughout the day (O'Neill *et al*, 2014 p.94; St James-Roberts & Hall, 1991) and many parents report that, while crying, their infants go red in the face, pull up their legs, or pass wind. These episodes normally resolve spontaneously within six months but may last much longer (Hide & Guyer, 1982; Rubin & Prendergast, 1984; St James-Roberts & Hall, 1991; Wurmser *et al*, 2001). Pinilla and Birch (1993) suggest that infants can learn to adapt their behaviour to their environment during the first three months and crying becomes more intentional and communicative as the baby develops. Over time parents develop an intuitive sense of what their infant's cry means and claim that they can distinguish normal from abnormal crying (O'Neill *et al*, 2014 p.94).

However, there is still a lack of clear diagnostic criteria, for both parents and health professionals, on when normal crying patterns become problematic crying patterns

(O'Neill *et al*, 2014 p.94). A number of terms have been used to describe what is perceived as abnormal crying which include colic, cry/fuss, fussing, infant irritability and excessive crying (Oberklaid, 2000). This terminology is vague and often used inconsistently, particularly when indicating degrees of severity of unsettled infant behaviour (Stark *et al*, 1975; Wessel *et al*, 1954). St James-Roberts and Wolke (1988) reported that they were able to distinguish between fussing and crying reliably, but this required specified training which was considered to be impracticable. Through qualitative in-depth interviews with nurses and parents of crying babies, three categories of cries were identified by Helseth & Begnum (2002) as follows. Firstly, the intense cry was described as attacks of hysterical, inconsolable crying in which carers assumed the infant was in pain. This was identified as 'real colic' and assumed to be due to a physiological cause such as gastrointestinal immaturity. Secondly, the non-specific fussing and crying was described as persistent and qualitatively normal. This cry was explained by infant and mother issues such as, temperament and maternal competence. Finally, parent identified feeding-related fussing and crying was explained by technical feeding problems. Though these criteria were based on the findings of a small sample, it offers some insight into mothers' perceptions of the range of causes of crying, which may be helpful in further research, particularly when differentiating normal crying patterns from abnormal crying.

The clinical experience of paediatric nurses suggests that the focus should be on the response to normal comfort behaviours rather than the quality of the cry itself, and proposes that if the infant responds to normal soothing tactics, the cry intensity is not significant (Fuller, 1996; Fuller, 1998). In addition, many of the parental diaries used for research data collection focus on infant crying duration but not on response to soothing techniques. A lack of consensus on the diagnosis of problematic crying demonstrates the complexities associated with both research in this field and supporting affected families.

2.3 Infantile colic

Infantile colic is the term most commonly used when referring to unsettled infant behaviour. Colic is a paediatric condition of unknown aetiology, described as a behavioural and non-pathological condition in early infancy with crying being the primary symptom. Colic affects up to about twenty-five percent of infants (de Weerth *et al*, 2013), corresponding with the prevalence estimates also reported for unsettled infant behaviour (Fisher *et al*, 2011; Hemmi *et al*, 2011; Hiscock & Jordan, 2004), though others report a prevalence of ten percent to forty percent of infants worldwide (Johnson *et al*, 2015). The most frequently used diagnostic criteria is the 'rule of threes' (Wessel *et al*, 1954), however many individual studies outline their own definition of colic which, combined with variation in study design, data collection method and sample size, may explain variations in reported prevalence (Leung & Lemay, 2004; Reijneveld *et al*, 2001; Stahlberg 1984). For the purpose of this section, a broad definition of colic, rather than the 'rule of three's', should be assumed unless otherwise stated.

Colic typically presents within the first four weeks of life and spontaneously resolves by three to four months of age (Barr, 1997; Gormally & Barr, 1997; O'Neill *et al*, 2014 p.95; St. James-Roberts *et al*, 1995; St. James-Roberts & Halil, 1991; Schmitt, 1985) mirroring an exaggerated form of the normal infant crying pattern. The typical crying associated with colic is characterised by prolonged bouts that tend to cluster in the late afternoon and evening, are difficult to soothe, and begin and end without apparent reason (i.e. paroxysmal and unpredictable) (Barr *et al*, 1992; Stifter & Braungart, 1992; St. James-Roberts *et al*, 1995; St. James-Roberts & Halil, 1991; Wessel *et al*, 1954). Some report that the child may draw up his or her legs, clench fists, arch his or her back and grimace as if in pain, but these symptoms are not necessary for colic to be diagnosed (Lehtonen *et al*, 2000). The incidence is equal between sexes (Johnson *et al*, 2015; Leung *et al*, 1997) and there is no correlation with type of feeding (breast versus bottle), gestational age, or socioeconomic status (Johnson *et al*, 2015). Colic is found more commonly in first-borns and infants with colic tend to have siblings who also had this condition

(Leung *et al*, 1997; Miller *et al*, 1989; Stahlberg 1984). The term 'colic' is used differently by parents, physicians and researchers (Barr, 1998; Barr, 2000; Barr *et al*, 1991; Canivet *et al*, 1996; Gormally & Barr, 1997) with the numerous hypotheses on the precise cause of infantile colic resulting in various approaches to treatment and no clear strategy for management (Lim, 2006).

The absence of consistent diagnostic criteria for colic constrains the synthesis of evidence on the effectiveness of interventions. Wessel *et al* (1954) developed the 'rule of threes' for diagnosing infantile colic. An infant is considered to have colic if he or she is otherwise healthy and well-fed, and has paroxysms of irritability, fussing or crying lasting for a total of more than three hours a day and occurring on more than three days a week for more than three weeks (Wessel *et al*, 1954). Yet, even with using these criteria, there is variation in reported prevalence. One study found only two percent of infants qualified as having colic when using Wessel criteria (Howard *et al*, 2006). In a prospective large scale study of Finnish infants, Lehtonen and Korvenranta (1995) estimated the prevalence of infantile colic at thirteen percent using Wessel criteria, though this study lacked consistency in the data collection time and method; two-thirds were questionnaires at three months post-partum and the remainder telephone responses at four to six months. One recognised limitation is that few parents or clinicians are willing to wait for three weeks to see if the increased crying will persist in order to meet the Wessel criteria for colic. More recently, an adapted form of the Wessel criteria has been introduced, the Rome III criteria, in which colic is defined as "episodes of irritability, fussing, or crying that begin and end for no apparent reason and last at least three hours a day, at least three days a week, for at least one week" (Hyman *et al*, 2006). Despite its salience for parents and clinicians, the behavioural syndrome of infant colic remains largely unexplained and without definitive diagnosis, an infant presenting with an acute episode of crying requires careful evaluation in order to ensure that a more sinister cause is not missed (Johnson *et al*, 2015).

Infantile colic is by definition a benign condition, diagnosis is made by exclusion of more concerning causes and parental support and reassurance are key components of management (Johnson *et al*, 2015). As the crying of infants with colic is understood as a signal of distress (Barr & Geertsma, 1993), continues to increase even with optimal caregiving (Barr, 1997; Miller *et al*, 1993; St. James-Roberts *et al*, 1998), and is associated with facial configurations thought to be related to pain (known as 'pain facies') (Barr *et al*, 1992), it is understandably taken to indicate that something is wrong or abnormal. Lehtonen *et al* (2000) propose that although the facial configurations tend to suggest pain, they may be features of more vigorous crying rather than diagnostic of colic.

Studies have demonstrated a significant difference between the crying duration of colicky and non-colicky babies. Hill *et al* (1992) showed two patient groups with colic had median total distress levels of 300 and 280 minutes compared with control infants who recorded a median total distress score of 102 minutes. Although the findings in this study were limited by the use of a twenty-four hour behaviour diary, which did not address longer term variation in signs of colic, they have been supported by other researchers (Barr *et al*, 1988; Barr *et al*, 1989; Forsyth, 1989; Hill *et al*, 1992; Lothe & Lindberg, 1989; White *et al*, 2000) who also demonstrated increased crying duration in colicky infants compared with non-colicky infants. The evidence, therefore, indicates the existence of colic as a condition despite the lack of clear identifiable causes.

Many aetiological factors for infantile colic have been explored including breast- versus bottle-feeding (Rubin & Prendergast, 1984), maternal demographic variables, socio-economic variables, parity, birth weight and other obstetric factors, but results have been conflicting and inconclusive (Hipperson, 2004). Some studies propose that excessive crying of infantile colic may be the primary sign of a gastrointestinal problem due to allergy to cows' milk (Forsyth, 1989), lactose intolerance (Miller *et al*, 1988; Moore *et al*, 1988), altered intestinal microbiota (Chau *et al*, 2015; de Weerth *et al*, 2013; Savino *et al*, 2010; Sung *et al*, 2014) or excess gas (Carey, 1984; Illingworth, 1985; Miller & Barr, 1991). It has also been suggested that colic may be a behavioural problem resulting from a less than optimal parent-infant interaction (Goldfeld *et al*, 2003), with the difficult temperament of the infant as a possible explanation for inappropriate parental reactions (Carey, 1984; Wolke *et al*, 1994). This raises the question of whether colic symptoms occur as a result of unhelpful care-giving responses to infants with difficult temperaments and unsettled behaviour, and more importantly, which problem comes first.

It is worth noting that a number of lines of evidence have led to reconsideration of the assumption that infantile colic is an 'abnormality' (White *et al*, 2000). Remarkably few infants with colic have been found to have organic disease (Gormally & Barr, 1997). Moreover, all the typical symptoms of colic syndrome are found in infants without colic, although they may be more marked, frequent, or intense in infants with colic. Additionally, the outcome for the infant is generally positive (Lehtonen *et al*, 2000; Lehtonen *et al*, 1994b; Stifter & Bono, 1998; Stifter & Braungart, 1992). Brazelton (1990) proposed transient developmental dysregulation of the nervous system as a cause of infantile colic. This is supported by suggestions that colic might be viewed as a clinical manifestation of normal emotional development and it could be regarded as merely the extreme end of normal crying (Barr, 1998b; Barr, 1991 p.55-61; Wolke *et al, 1994*). Indeed, it has been suggested that colic should be renamed as 'variant of normal infant behaviour' (VONIB) (Armstrong *et al*, 2000). Of note is that in some underdeveloped communities, the term 'infantile colic' is virtually unknown (Thomas, 1981). Wessel *et al* (1954:p.428), whose criteria for colic is most often referred to, anticipated the similarities between the clinical problem of colic and normative crying patterns by making the observation that "the time distribution and frequency of diurnal regularity are similar for the mild fussy periods of the 'contented babies', and for the more prolonged periods of the 'fussy infants'".

2.4 Chapter summary

Unsettled infant behaviour is a problem of significant proportions which, although is researched mostly among developed and educated societies, broadly the pattern of behaviours is found to be similar cross-culturally. The rate of unsettled infant behaviour is wide ranging from twenty to thirty-five percent of infants (Hogdall *et* *al*, 1991) and this may be attributable, in part, to the difficulty in precisely defining the condition and its aetiology. The different use of terms when referring to unsettled infant behaviour, along with inconsistent definitions, presents an issue throughout the literature. Infantile colic, a term commonly associated with unsettled infant behaviour, is defined mostly but not exclusively by using the Wessel 'rule of three's' criteria. Using different criteria for colic impacts reports on prevalence, cost implications and treatment effectiveness of this condition. Even differentiating problematic crying from normal crying patterns has proven difficult. This thesis will retain the term 'unsettled infant behaviour' throughout, except when referencing other researchers where the original terminology in that reference will be used.

The prevalence of unsettled infant behaviour is also influenced by parents' perceptions of the intensity and duration of crying bouts, the method by which data on crying are collected, the psychosocial wellbeing of the parenting couple and culturally determined infant care practices (Fleisher & Barr, 2008). Apparently, babies around the world start to cry with similar frequency; what varies is the length of crying after onset of fussiness and the comforting response patterns from culture to culture and between parents within a cultural group (Fleisher & Barr, 2008). In spite of decades of research much remains unknown, and that which is known is often contradictory and inconclusive.

The next chapter explores some of the suggested aetiologies of unsettled infant behaviour; e.g. gastro-oesophageal reflux disease (GORD) or 'reflux', cow's milk protein allergy (CMPA), lactose intolerance and gut irritability. Diagnostic approaches and management strategies for each of these conditions will be described and the effectiveness of treatment protocols will be examined in terms of unsettled infant behaviour.

Chapter 3 - Gastrointestinal problems and unsettled infant behaviour

Unsettled infant behaviour is a problem of significant proportions for which no known cause has been definitively identified. Inconsistent use of terminology and poor categorising of normal crying behaviours contribute to some of the confusion experienced by parents trying to manage unsettled infants. When reviewing the literature on unsettled infant behaviour, although different terms are used, the one most commonly found in studies is ‘infantile colic’. Regardless of the long established Wessel criteria (1954) for infantile colic, this term is often ill-defined in individual research studies, making comparison of results difficult to establish. For this reason, although the term used in individual studies will be the one reported on, the term used by the researcher throughout the thesis will be ‘unsettled infant behaviour’.

The involvement of various gastrointestinal pathologies have been suggested causes of unsettled infant behaviour. This chapter identifies the gastrointestinal conditions of particular interest; which include gastro-oesophageal reflux, cow’s milk protein allergy, lactose intolerance and gut irritability. Each condition will be examined with reference to their association with unsettled infant behaviour and the strength of evidence available. In spite of much research, the conclusions are often contradictory and of primary concern is the weakness of diagnostic criteria which can affect the prompt implementation of appropriate management strategies. Finally, a growing support for the role of probiotics is presented and linked to recent studies into the gut microbiota of unsettled infants.

3.1 Reflux

Gastro-oesophageal reflux disease (GORD or GERD), more commonly referred to as ‘reflux’, is one of the most common paediatric medical disorders of the gastrointestinal tract. Diagnosis is usually based on patient history and physical examination. According to Douglas (2005) it has become common for an infant who cries excessively, and vomits, to be labelled as having reflux. However, the diagnosis of GORD in otherwise healthy, full-term infants with persistent crying under three months of age is often mistaken (Vandenplas *et al,* 2007; Sherman *et al,* 2009; Van der Pol, 2011) and can easily be confused with the symptoms of colic (Douglas & Hiscock, 2010; Lim, 2006). On clinical grounds it may be difficult to assess whether GORD is within physiological limits, without resorting to invasive procedures not available outside the hospital setting and not routinely done on infants under three months of age (Lim, 2006), such as oesophageal pH monitoring or endoscopic biopsy (Heine *et al*, 2002; Vandenplas *et al,* 2004). Only one-sixth of infants with persistent crying have a diagnosis of pathological GORD confirmed by pH monitoring (Heine *et al*, 2006). Prevalence reports can vary greatly depending on recruitment methods, PH monitoring techniques and diagnostic cut-off levels, which makes direct comparisons between studies difficult (Vandenplas *et al,* 2004). As a result, the diagnosis of reflux is often controversial, particularly when distinguishing between GORD and physiological regurgitation and deciding when intervention and/or medication is indicated.

Differentiating between pathological GORD and physiological regurgitation is necessary when considering a management plan in affected infants. Vandenplas *et al* (2013) conducted a thorough literature review and found distinct differences between physiological gastro-oesophageal reflux (GOR) and gastro-oesophageal reflux disease (GORD). GOR is common in infants and affects forty to sixty percent of those aged between one and four months (Henry, 2004). GOR is a benign physiologic process that allows retrograde flow of gastric content into the oesophagus and is thought to be caused by immaturity of the oesophagus (Cezard, 2004). Physiological regurgitation may occur frequently in the first few months of life (Sherman *et al*, 2009) but the infant is generally content and thriving. It has been observed that the presence of regurgitation is related to the volume of food ingested: the larger the volume ingested, the longer the gastric emptying time, the higher the intra-gastric pressure, and the more frequent the transient spontaneous relaxations of the lower oesophageal sphincter, all of which predispose an infant to gastro-oesophageal reflux (Khoshoo *et al*, 2000). It is not associated with any complications and these infants are often referred to as 'happy spitters' (Henry, 2004). The management of physiologic regurgitation includes parental education regarding conservative management techniques (elevation, positioning, feeding techniques) and the use of thickened anti-regurgitation (AR) formula in some cases. There can be a tendency to prescribe medication, especially if the infant also presents with unsettled behaviour, but there is no evidence for the use of anti-secretory drugs or prokinetic agents in infants with physiologic regurgitation (Heine *et al*, 2006; Vandenplas *et al*, 2013).

In contrast, pathological GORD is thought to involve the simultaneous contraction of the rectus abdominis muscle during lower oesophageal sphincter relaxation causing the propulsion of gastric contents into the oesophagus, which present as overt regurgitation (Kawahara *et al*, 2001). These infants present with crying and fussing during feeds, irritability after feeds, vomiting, weight loss and respiratory symptoms (Henry, 2004). These signs are perceived to be useful clinical markers of pathological GORD (Mathisen *et al*, 1999). But the diagnostic accuracy of these clinical signs has not been prospectively tested (Heine *et al*, 2006) and they are neither sensitive nor specific for the diagnosis of GORD (Heine *et al*, 1995; Jordan *et al*, 1999).

According to some researchers the majority of GORD cases settle with growth and development of the infant or conservative management and only a small percentage of infants require medication or surgery (Armstrong *et al*, 2000; Vandenplas *et al*, 2013). Although H2 antagonists and omeprazole have proven efficacy in the management of severe GORD in infancy and childhood, there continues to be concerns regarding the effect of prolonged acid suppression in infancy (Armstrong *et al*, 2000). Reported adverse outcomes of pharmaceutical interventions include fatal cardiac arrhythmias secondary to the previously widely prescribed prokinetic agent, cisapride (Augood *et al*, 2003), and elevated plasma aluminium levels secondary to antacid therapy (Vanderplas *et al*, 2009). If GOR, pathological or physiological, is the suspected cause of unsettled behaviour in infants, every effort should be made to address this through conservative management techniques before embarking on pharmaceutical or surgical intervention that may bring unnecessary additional complications (Armstrong *et al*, 2000). This is particularly important in cases where definitive diagnosis of GORD is outstanding and other causes of unsettledness have not been ruled out.

3.2 Cows Milk Protein Allergy

Intolerance to cow's milk or other food proteins ingested either via the mother's diet and breast milk, or from infant formula has been proposed as a cause for unsettled behaviour in babies (Vandenplas *et al*, 2013). Only eight foods (cow's milk, soy, hen's eggs, peanuts, tree nuts and seeds, wheat, fish and shellfish) account for ninety percent of all food allergies. Cow's milk protein allergy/intolerance (CMPA/CMPI) is the most common food allergy in early childhood with an incidence of two to three percent in the first year of life (Host, 2002). CMPA has a good prognosis, with over eighty percent full recovery by three years of age (Host *et al*, 1995).

CMPA is associated with unsettled infant behaviour; in fact it is suggested that CMPA may be a real, albeit rare, cause of infantile colic (Barr, 1996; Gormally & Barr, 1997; Hill *et al*, 2005; Lucassan *et al*, 1998; Miller & Barr, 1991; Treem, 1994). This theory is supported by reports that the symptoms of colic improve when a cow's milk-free diet is implemented (Hill *et al*, 1995; Hiscock & Jordan, 2004; Lothe *et al*, 1982; Lothe & Lindberg, 1989; Lucassan *et al*, 1998). Lozinsky and Morals (2014) concluded in their recent review of the literature that CMPA can cause eosinophilic colitis which, in turn, causes unsettled infant behaviour in the first six months of life. A relationship between GORD and CMPA is also suggested with fifteen to twenty-one percent of children who suffer from one of the conditions found to also suffer from the other and sixteen to forty-two percent of children with a history of GORD showing symptoms of CMPA (Vanderplas *et al*, 2007). In fact, Merwat & Spechler (2009) hypothesise that proton-pump inhibitors for the treatment of GORD may predispose to food allergies, which emphasises the importance of clear differential diagnosis for GORD before medicating.

Many studies on cow's milk protein (CMP) have not investigated the immunological basis of the clinical reactions (Host *et al*, 1995); tests available have low sensitivity (some less than thirty percent) and low positive predictive value (Costa *et al*, 2011) and often the terms CMPA and CMPI are used synonymously. It is suggested that sixty percent of reactions are IgE mediated, with casein and whey proteins accounting for eighty percent and twenty percent respectively (O'Neill *et al*, 2014 p.133). Non-immunological reactions against CMP are defined as CMPI. The diagnosis for CMPA is often dependent on clinical appraisal (Forsyth *et al*, 1985, Vandenplas *et al*, 2007) and should be suspected in an infant with recurrent regurgitation who also has eczema and/or wheezing (Vandenplas *et al*, 2013). Other signs are reddening of the skin if touched by the food, blood-stained mucous in the stool, presence of a positive family history for atopic disorders (Nocerino 2015) and failure to thrive (Fisher *et al*, 2009). These signs may be accompanied by crying, but crying alone is not a sufficient diagnostic sign of a food allergy or intolerance (Liebman, 1981).

An elimination diet by a double-blind placebo controlled food challenge is the gold standard for diagnosis (De Greef *et al*, 2012; Koletzko *et al*, 2012). CMPA is confirmed when there is complete resolution of symptoms after CMP is eliminated and recurrence of symptoms within forty-eight hours once CMP has been reintroduced; thus making a clear association between the unsettled behaviour and the ingestion of CMP. Nocerino *et al* (2015) provide a systematic review of the most recent evidence on the pathogenesis of clinical and diagnostic aspects of food allergy-induced infantile colic and suggest a stepwise diagnostic approach so that misdiagnosis and inappropriate actions can be avoided.

The changing of infants' normal food is the suggested treatment protocol in formula fed infants suspected of having CMPA, with soy-based formula or extensively hydrolysed formula (EHF) being suggested alternatives. In a long-term prospective study, Iacono *et al* (1991) reported immediate remission of symptoms in fifty out of seventy infants given soy-based formula in place of their regular CMP formula. No control group was used in this study and it was not blinded, leaving a risk for bias. The results are further weakened by potentially misleading conclusions where the authors report that eight of the fifty infants regarded as responding to the CMP free diet, subsequently also became intolerant to the soy-based substitute. A relapse in symptoms due to misdiagnosis of CMPA should have been a consideration and would have changed the reported outcome of the study results. In a small scale study Campbell (1989) reported complete resolution of what they describe as 'infantile colic' in thirteen out of nineteen babies (sixty-eight percent) with dietary change to soy-based formula, though there was a conflict of interest in this study as it was part-funded by a formula milk supplier. Conflicting results have been reported for the use of soy-based formula (Berseth *et al*, 2009; Lothe *et al*, 1982; Forsyth *et al*, 1985). In 2008, the American Academy of Pediatrics stated that "the routine use of isolated soy protein-based formula has no proven value in the management of IC (infantile colic) or fussiness" (Vandenplas *et al*, 2013). Due to recent reports of the nutritional disadvantages of soy-based formulas, it is now not recommended in subjects aged under six months and EHF is recommended instead (Nocerino *et al*, 2015). There is also a variable degree of observed improvement in symptoms of unsettledness and colic when using EHF. As there is a wide range of available infant formulas with little guidance on appropriate use, care should be taken before changing infant food. The availability and ease of use of alternative formulas may lead to the over-diagnosis of CMPA and the possibility of other diagnoses being missed (Campbell, 1989).

In breastfed infants, a CMP free diet for the mother is recommended. The level of CMP in breast milk is 100,000 times lower than that in cow's milk formula and therefore CMPA is believed to be much less common in breastfed infants compared with formula fed infants (Host *et al*, 1990). A high quality randomised controlled trial reported an absolute risk reduction of thirty-seven percent (95% confidence interval: 18-56%) in breastfed infant's cry/fuss duration when mothers changed from a control diet to a hypoallergenic diet (eliminating dairy foods, eggs, peanuts, tree nuts, wheat, soy and fish) for seven days (Hill *et al*, 2005). Jakobsson & Lindberg (1978) reported twelve out of eighteen breastfed babies with colic were rendered symptom free by elimination of cow's milk from the mother's diet, though the data was weakened by being a small sample with no control. Similar to the studies on formula fed infants, conflicting results are reported for CMP elimination in the mother's diet of breastfed infants.

Vanderplas *et al* (2007) developed a set of guidelines for managing CMPA in infants. They emphasised the importance of continuing breast-feeding where possible as only 0.5% of exclusively breastfed infants showed reactions when challenged with CMP, and most of those were mild to moderate. This was supported by an earlier study, which found that the elimination of cow's milk from the mother's diet had no effect on the duration of colic in breastfed infants (Evans *et al*, 1981). One could conclude, therefore, that in both breastfed and formula fed infants, unless complete remission of unsettled and colicky symptoms is achieved through the CMP free diet, normal feeding practices should be resumed without delay and persistence of unsettled behaviour should be explored further.

3.3 Lactose Intolerance

Lactose intolerance has been implicated in unsettled infant behaviour but, like GORD and CMPA, it can be difficult to diagnose, often relies on clinical judgement (Campbell, 1989) and its role remains uncertain (Hiscock & Jordan, 2004). It has been hypothesised that some babies have a transient underlying lactase deficiency, leading to a build-up of lactose derived from breast milk or formula (Hiscock & Jordan, 2004). Diagnosis of lactose intolerance involves testing for faecal-reducing substances. However, Liebman (1981) found no association between babies with colic and lactose intolerance, as measured by stool pH and reducing substances. Breath hydrogen testing is thought to be a more sensitive indicator of incomplete lactose absorption in the small intestine (Levitt, 1969). Lactulose is a quantitatively non-absorbable carbohydrate, which contains lactose. Increased breath hydrogen excretion after an oral load of lactulose may represent increased lactose malabsorption, differences in colonic bacterial fermentation conditions, or differences in the handling of colonic gas produced (Hyams *et al*, 1989). Some researchers have reported that colicky infants produce more breath hydrogen in the fasting state and in response to feedings containing lactose (human milk and commercial formula) than non-colicky infants (Miller *et al*, 1989; Moore *et al*, 1988) though both these studies should be regarded with caution. Miller *et al* (1989) lacked a clear criteria for identifying infants with colic, the study was not blinded or randomised and the age of the controls was older than the study group making comparison of results difficult. Moore *et al* (1988) demonstrated a high incidence of colic (sixty-eight percent) in normal infants fed milk containing lactose by using a broad definition of colic, which included milder symptoms that would otherwise be excluded in the majority of studies. Barr *et al* (1984) have shown that there is a spectrum of increased breath hydrogen in normal babies, and that hydrogen excretion has a similar monthly timing pattern to that of infant colic. By delivering a standardised lactulose load to the colonic flora of colicky and non-colicky infants, Hyams *et al* (1989) found no difference in breath hydrogen levels between colicky infants (> 3 hours crying/day) and controls (< 3 hours crying/day), therefore, undermining the suggestion that colicky infants produce more hydrogen from mal-absorbed carbohydrate than non-colicky infants. Although this was a small study, the criteria for colic was better defined than previous studies (Moore *et al*, 1988) creating a clear distinction between test and control groups for comparison of outcomes. The validity of this assumed causal relationship between intestinal gas production and unsettled infant behaviour, or colic, requires further evaluation.

When treating infants with lactose intolerance one recommendation is to change to a lactose free diet. Lactose-free formula is readily available and a clinical response confirms the diagnosis. For breastfed babies, the use of lactase drops is thought to help (Hiscock & Jordan, 2004) although there are mixed reports of the benefits. In a double-blind, placebo-controlled, crossover study of forty-six infants with excessive crying and diarrhoea, treating breast milk or formula with lactase drops resulted in significantly less crying (AAP, 2000). However, Miller *et al* (1990) reported that lactase drops had no significant effect on the duration of crying in breastfed infants, when the lactase was given directly into the babies' mouths during a breast-feed. Hydrogen excretion was not reduced in the treated group in Miller's study, suggesting that the lactase had been inactivated in the stomach. In Hiscock & Jordan (2004) literature review they suggest that for breastfed babies, expressed breast milk needs to be pre-treated with lactase drops for twelve to twenty-four hours and then given to the baby in a bottle. This approach is inconvenient for breast-feeding mothers and may even risk the cessation of breast-feeding. Without a confirmed diagnosis and definitive reduction in unsettled behaviour in response to treatment, the use of lactase drops in expressed breast milk would be regarded as unnecessarily cumbersome and inadvisable, and other possible causes for the infants' unsettled symptoms would need consideration (Douglas, 2013).

3.4 Gut irritability

Functional gastrointestinal symptoms are frequent in infants (Hyman *et al*, 2006). Intestinal hormone abnormalities have been a suggested cause of infantile colic with research into associations with increased serum levels of motilin in cord blood (Lothe *et al*, 1990b), hypocontractibility of gall bladder (Lehtonen *et al*, 1994b) and increased serotonin levels (Kurtoglu *et al*, 1997) in infantile colic. Lothe *et al* (1990a) found that S-motilin is one of several gut hormones involved in increasing modulation of the gut motility and is higher in colicky infants than non-colicky. S-motilin is also higher in formula fed infants with colic compared with breastfed infants with colic. In addition, breastfed and formula fed infants with colic were found to have an increased transmission of the macromolecular human alpha (α)-lactalbumin across the gut compared with healthy, non-colicky, age-matched infants, demonstrating abnormal function of the gut mucosa in the colicky infants (Lothe *et al*, 1990a). According to Lehtonen *et al* (1994b) infants with colic have hypocontractility of the gall bladder, which indicates abnormal biliary tract physiology and is associated with infantile colic.

The management of gut irritability in colicky babies can be problematic. In a systematic review, Lucassen *et al* (1998) reported that the anticholinergic drug, dicyclomine hydrochloride, reduced the symptoms of colic but had serious side effects and is, therefore, no longer recommended. Other interventions for treating gut irritability have mixed responses. Despite anecdotal reports of its benefits, the use of simethicone (or Infacol drops) for wind has been found to have no effect on infant crying or irritability when compared with placebo (Garrison & Christakis, 2000; Lucassen *et al*, 1998). Many other remedies and treatments are used in attempts to alleviate the baby's distress but the evidence to support these are poor (Lucassen *et al*, 1998).

Recently, there is increased research into the use of probiotics for colic. Probiotics are defined as "live microorganisms that, when administered in adequate amounts, confer health benefits on the host." (WHO, 2001). According to Chau *et al* (2015) infants with colic may display inadequate levels of lactobacilli in early infancy, which affects intestinal fatty acid profiles, and are more frequently colonised with the gas-forming *Clostridium difficile*, *Escherichia spp*, and *Klebsiella spp*. Supporting this theory, Rhoads *et al* (2009) explored whether gut inflammation, colonic fermentation, and/or an altered colonic flora could provide a pathophysiological mechanism for colic and demonstrated elevated levels of fecal calprotectin and higher levels of *Klebsiella* in infants with colic. Early epidemiological studies have shown that the acquisition and development of the intestinal microbiota is a complex process (de Weerth *et al*, 2013). It is influenced by various factors, including mode of delivery, drug exposure, nutrition and feeding type, stress, degree of hygiene and infections; all of these factors play a central role in the development of allergic diseases (de Weerth *et al*, 2013). In their systematic review, de Weerth *et al* (2013) found that infantile colic was related not only to an atypical colonisation pattern, but also to the lack of microbial diversity of the intestinal microbiota in the early days of life.

Some recent studies have reported the benefits of probiotic, Lactobacillus reuteri DSM 17938, in the treatment of unsettled infants and colic (Chau *et al*, 2015;

Savino *et al*, 2010; Szajewska *et al*, 2013). Savino *et al* (2010) reported fifty breastfed infants (twenty-nine boys) with colic, where the benefit of supplementation with the probiotic Lactobacillus reuteri DSM 17938 was clearly demonstrated by a significant reduction in daily crying time. Microbiological analysis of the infants' faeces revealed a modification in gut microbiota which could be involved in the observed clinical improvement. The effect of administered Lactobacillus reuteri DSM 17938 on fifty-two exclusively breastfed infants diagnosed with colic was demonstrated by Chau *et al* (2015), with a significant reduction in daily crying and fussing times when compared with placebo. These findings were supported by Savino *et al* (2010) where the benefit of supplementation with the same probiotic was clearly demonstrated on fifty breastfed infants with colic. Similarly, in a RCT by Szajewska *et al* (2013), eighty infants aged under five months with infantile colic (using Wessel criteria), who were exclusively or predominantly breastfed (>50%) were randomly assigned to receive *L reuteri* DSM 17938. These researchers found that crying time was significantly reduced in the probiotic group compared with the control group. All studies were double-blinded, randomised, placebo-controlled trials.

Yet Sung *et al* (2014) failed to demonstrate positive probiotic effects in 167 breastfed and formula fed infants with colic. According to Sung *et al* (2014), it is possible that infants with allergic disease have different gut microbiota according to different geographical locations, even among countries with westernised lifestyles. They suggest that the differences observed in the effect of Lactobacillus reuteri may be attributed to the differences in colonisation pattern and stability of the intestinal microbiota of infants from Australia, Italy, Poland and Canada. These are new theories and to date there is no supporting evidence. Continuing the trials across different regions is important to establish if infants from one area may be more susceptible to the effects of specific probiotics than other regions. The laboratory analyses used to detect the characteristic microbial signatures of infants with colic are presently too complex, time consuming and expensive for application as a diagnostic screening instrument.

3.5 Chapter summary

When an infant presents with unsettled behaviour there are many potential causes and a systematic approach to diagnosis is lacking. Identifying which infantile condition may be causing the unsettled behaviour is problematic due to the common presentation of associated symptoms. These can include persistent crying, 'pain facies', drawing the knees up, regurgitation, abdominal bloating and excess wind; a combination of which can be found in colic, reflux, CMPA, lactose intolerance and gut irritability. While the primary complaint is often persistent and inconsolable crying, crying alone is not sufficient to make any single diagnosis. What is clear from the literature is that organic disturbance is implicated in only a small percentage of cases, but due to the distress placed on families there is a risk of misdiagnosis which, in turn, may result in incorrect management protocols that can be harmful. The situation is further complicated by inaccurate and unreliable diagnostic testing protocols leaving much of the decision making to clinical judgement. In addition, there is generally poor cross-professional communication and a lack of consensus about how to diagnose and manage infants with unsettled behaviour, which causes much confusion and frustration for parents.

The clearest indicators to date on the management of unsettled infant behaviour focus on a multidisciplinary approach to support, information and education with particular emphasis on parental expectations and infant handling advice. In chapter 4, the regulatory disordered infant is described. In addition, how regulatory problems, especially in feeding and sleeping, interact with each other and the impact on infant behaviour is discussed.

Chapter 4 - Regulatory problems and unsettled infant behaviour

Unsettled infant behaviour is recognised as a highly prevalent problem which continues to cause concern and anxiety for parents and confusion for health professionals. The large body of research addressing this phenomenon has failed to identify a clear diagnostic process and the methodological rigor of these studies has been questioned (Cook *et al*, 2012). In previous chapters, alternative terms for unsettled infant behaviour, i.e. problematic crying and colic, were presented and the conditions most frequently regarded as contributing factors to unsettled infant behaviour such as reflux, CMPA, lactose intolerance and gut irritability, were examined. However, a lack of consistent multidisciplinary consensus has only succeeded in further complicating the decision-making practices and studies examining changes to diet or use of medication often yielded no effect over placebo (Cook *et al*, 2012).

The possibility that unsettled infant behaviour is not a consequence of organic disturbance within the infant needs consideration; it may be connected to alterations in an infant's natural regulatory development. The presenting symptoms of unsettled infant behaviour include excessive episodes of crying, inconsolable crying, resistance to soothing, feeding problems, difficulties settling to sleep, waking after short sleeps, and frequent overnight waking (Fisher *et al*, 2011). These behaviours, when linked together, are sometimes referred to as infant regulatory problems (DeGangi *et al*, 2000; Forsyth & Canny, 1991; Hemmi *et al*, 2011; Von Hofacker & Papousek, 1998; Wolke *et al*, 1995) and an infant can present with one or several of the symptoms.

In this chapter, the 'regulatory disordered infant' is introduced and how regulatory processes in infant development can be disturbed is discussed, particularly in relation to sleeping and feeding problems. There is some examination of regulatory problems in early infancy as a predictor of later issues, and how these links may be exaggerated. The ability of infants to self-regulate, how this process can be supported and the evidence that suggests why some infants achieve this better than others, is presented. As stated in earlier chapters, one major challenge when reviewing the literature on unsettled infant behaviour is the variety of terms and definitions used by different authors in individual studies. Although always referring to unsettled infant behaviour in this document, the original terminology used by the authors will not be changed when referencing their studies.

4.1 The 'regulatory disordered infant'

The belief that crying, feeding and sleeping behaviours are related in infancy is held by many parents and physicians (Oberlander *et al*, 1992). DeGangi *et al* (1991) proposed that infants who manifested two of the following persistent problems at five months: a crying problem (cry duration > 2 hours/day or difficult to soothe), a feeding problem (vomiting, problem with drinking, or flatulence) or a sleeping problem (night waking), should be considered to have the diagnosis 'regulatory disordered infant', which presumes significant co-morbidity of increased crying, sleeping or feeding problems.

The significance of co-morbidity between increased crying, sleeping and feeding problems was investigated by Wolke *et al* (1995) in a prospective community study of a representative sample of infants. A normative randomly chosen sample was studied longitudinally and parents received a standardised interview from paediatricians regarding crying, sleeping and feeding behaviours. Although an association between infants with increased crying and mothers who were anxious about infant sleep behaviour was identified, no significant co-morbidity of cry duration with either sleeping or feeding problems was found. Whether these infants were inherently physiologically regulatory disordered (DeGangi *et al*, 1991) or caretaking practices mitigated against behavioural organisation of these infants could not be concluded with certainty (Wolke *et al*, 1995). This study was limited by being based on parent interviews when studies have shown that more reliable data can be obtained by using infant behaviour diaries (e.g. Barr *et al*, 1988). Measurement methods for infant behaviour are discussed in more detail in chapters 7 and 8.

A relationship between regulatory problems and both infantile colic (White *et al*, 2000) and infant temperament (Buss & Plomin, 1984; Rothbart, 1986) has been suggested. Keefe *et al* (2006) proposed a relationship between psychobiological disturbance in infant behaviour regulation due to increased sensitivity to the environment and infantile colic. They suggested that disruptions or inconsistencies in parenting, or the surrounding environment, overstimulate the infant resulting in crying that the infant does not yet have the maturity to regulate. In a RCT by Keefe and colleagues (2006), nurses visited families of the intervention group (n = 64) four times over one month to provide support to parents, make modifications to infant care (with an emphasis on consistency of routines) and educate parents on reducing overstimulation in their infant. Compared with the control group (n = 57) who received usual care, intervention infants had a significantly higher number of resolved crying problems as well as shorter total crying time/day at thirteen weeks of age. This data suggests that intensive parental support, modification of environment and provision of structured care can reduce crying.

Prolonged crying is described as crying that persists beyond thirteen weeks (Vik *et al*, 2006). Prolonged crying should not be confused with infantile colic as it is markedly less prevalent and likely to have a different aetiology (Vik *et al*, 2006). Rao *et al* (2004) demonstrated this differentiation in a longitudinal study on over 400 infants, and reported that although colic was not associated with long-term effects on childhood cognition, excessive crying that persists beyond three months of age in infants without other signs of neurological damage may be a marker for cognitive deficits during childhood. In studies in which cases were defined by prolonged crying beyond the normal crying peak, as well as multiple areas of problematic behaviour, the findings should be regarded with caution as generalised regulatory disturbances (attention-deficit⁄hyperactivity disorder) with adverse long-term psychological and behavioural disturbances cannot be ruled out (Papoušek & von Hofacker, 1998; Rao *et al*, 2004; Schmid *et al*, 2010; Wolke *et al*, 2002).

There were very early reports of involvement of the autonomic nervous system and parasympathetic imbalance in regulatory problems (Eppinger & Hess, 1915; Jorup, 1952; Wessel *et al*, 1954) and psychophysiological research identified a pattern of autonomic hyper-reactivity in regulatory-disordered infants (DeGangi *et al*, 1991; DeGangi *et al*, 2000). An aetiology considered by Wessel *et al* (1954) for colic was congenital imbalance of the autonomic nervous system causing a 'hypertonic infant'. In relation to the hypertonic infant Haas (1918) stated, "It is characterized by hypertonicity of all the skeletal muscles, as shown by the ability to raise the head and grasp objects even in the early days of life, and by general spasticity…There is marked psychic irritability, expressed by insomnia, general restlessness and crying.” This is supported by the concept of ’Vagotonia‘, described by Eppinger and Hess in 1915, who postulated that because of abnormal sensitivity of the central nervous system, minimal stimuli, which are usually without effect lead to the development of fussiness in certain infants. However, research in this area is dated and more recent studies have mainly focused on the interactions between sleeping and feeding regulation in infants and effects of disorganised patterns on infant behaviour.

4.2 Sleep dysregulation

In the first six months of life, between fifteen and thirty-five percent of parents report a problem with their infant’s sleep, which affects the perception of infant behaviour (Goodlin-Jones *et al*, 2001; Messer & Richards, 1993). Difficulties include settling their infant to sleep at the start of the night and re-settling them overnight (Goodlin-Jones *et al,* 2001). A key issue is that contrary to parental reports, most infants continue to wake up in the night by three months (Goodlin-Jones *et al*, 2001). However, some infants signal to their parents upon waking rather than resettling autonomously (Anders *et al*, 1992; Goodlin-Jones *et al*, 2001; Minde *et al*, 1993). The unsettled nature of this sleep pattern is, therefore, associated with an inability to self-settle from normal intermittent night-time waking.

Dispute exists about the coexistence of infant crying and sleep problems, and whether one causes the other. Weissbluth (1981) reported that concurrent total sleep duration of infants who cry excessively, referred to in this paper as ‘temperamentally difficult’, is significantly shorter in comparison to ‘easy infants’ or normative criers. However, this was an observational study with a risk of bias, as all scoring and comparisons were carried out by the researcher. Further research on crying and sleep carried out by Weissbluth and colleagues (1984b) found associations between retrospective reports of colic (using Wessel criteria of crying patterns) and more frequent night waking in infants at four to eight months. This study relied on parental recall of infant crying that occurred months earlier and the population in this study lacked generalisability, being from white middle-upper class families. Yet the findings were supported by other researchers who have shown that infants with colic sleep less than infants without colic (Papousek & von Hofacker, 1995; St James-Roberts *et al*, 1997) and that excessive infant crying is associated with subsequent childhood sleeping problems (Rao *et al*, 2004; Schmid *et al*, 2010; von Kries *et al*, 2006). Weissbluth (1987) suggested that congenital biological factors, which lead initially to colic can persist to cause later sleep disturbance. However, other researchers found a weak relationships between fuss/cry problems in the early months and sleeping problems at eight to twenty-four months of age (St James-Roberts & Plewis, 1996; Wake *et al*, 2006). Moreover, it has also been suggested that colic might be as a result of sleep deprivation or dysregulation (Papoušek & von Hofacker, 1998; White *et al*, 2000).

Although an association has been made between early infant crying and subsequent sleep disturbance, the relationship is not clear and it is important to distinguish one from the other (St James-Roberts & Plewis, 1996). Crying usually peaks at five to six weeks (Barr, 1990b; St James-Roberts, 1989; St James-Roberts, 2001) whereas sleep complaints start after twelve weeks (Adams *et al*, 2004; Lozoff *et al*, 1985; Messer & Richards, 1993), which is possibly because up to this point parents expect to be awoken at night (St James-Roberts, 2008). There is evidence to suggest that infants who do not stop signalling for parental attention during the night by five months of age are more likely to develop chronic sleeping problems (Papoušek & von Hofacker, 1998; Wolke *et al*, 1995).

In a recent study, St James-Roberts & Peachey (2011) assessed the prospective relationship between excessive crying at five to six weeks and infant night waking with signalling at twelve weeks of age. Data from two separate longitudinal studies were analysed (Nikolopoulou & St James-Roberts, 2003; St James-Roberts *et al*, 2006); infant crying data were obtained from validated behaviour diaries and sleep-waking data from standard parental questionnaires. Infants who remained settled for five hours or more without signalling parents at twelve weeks of age was the criteria used to measure settled infant sleep-waking as in previous studies

(Nikolopoulou & St James-Roberts, 2003; Pinilla & Birch, 1993; St James-Roberts *et al*, 2001). Both studies showed a reduction in crying amounts and number of colic cases between six and twelve weeks (Nikolopoulou & St James-Roberts, 2003; St James-Roberts *et al*, 2006). The majority of infants who met criteria for excessive crying or colic at five to six weeks of age were settled in the night at twelve weeks of age, and 'excessive criers' were not more likely than other infants to wake and signal parents in the night at twelve weeks (Nikolopoulou & St James-Roberts, 2003; St James-Roberts *et al*, 2006). Therefore, it was concluded that excessive crying and sleep-waking problems have different causes (St James-Roberts & Peachey, 2011). These findings were supported by another study of 120 low-risk, full-term infants from a middle class sample, which demonstrated using parental report diaries, that sleep–waking behaviour and difficult temperament were notably stable from early infancy to toddlerhood, but independent of each other in this cohort (Hayes *et al*, 2011).

St James-Roberts & Peachey (2011) suggested that infants' sleep-waking problems usually involve normal developmental processes and environmental factors, which maintain signalling behaviours rather than a generalised disturbance. This is also consistent with previous assertions that so-called 'post-colicky' sleep problems are likely to be due to a failure of the parents to establish and maintain regular sleep schedules (Carey, 1989; Thomas and Chess, 1977; Weissbluth *et al*, 1984a; Wolke *et al*, 1995). Maternal perceptions and expectations about infant sleep are strongly related to infant sleep problems (Morrell, 1999). Parents who have problems resisting their infant's demands, who rock, feed, or remain with their infant while the infant falls asleep, are more likely to report frequent night awakenings and settling problems (Hiscock, 2010). Such problems have been consistently linked to parental mood disorder (Field *et al*, 2007; O'Connor *et al*, 2007) and when infant sleep problems are treated, parental depressive symptoms decrease (Armstrong *et al*, 1998b); this is discussed in greater detail in chapter 5.

From birth, parents play an important role in the development of their infant's sleep patterns. Although co-sleeping in the early stages has been linked to less cry/fuss behaviours, it has also been connected with sleep disturbances later on (St James-Roberts, 2008). Co-sleeping and frequent breastfeeding, the usual caretaking practice in most non-western societies, are often distressing to mothers in western societies, where such practices are frequent but not the norm (Barr, 1990a). In a comparative study, St James-Roberts and colleagues (2006) collected evidence about methods of parenting and associated infant crying and sleeping in two communities with substantially different approaches to infant care; London, United Kingdom where a 'scheduled' approach to infant care was the primary practice and Copenhagen, Denmark where 'infant-demand' care was more popular. The findings from these two communities were compared with a third group who practiced 'proximal care', where parents planned to hold their infants for more than eighty percent of the time between 8am and 8pm, breastfeed frequently, and respond rapidly to infant cries. London parents had fifty percent less physical contact with their infants than proximal care parents, including less contact when the infants were crying and when awake and settled. London parents also abandoned breastfeeding earlier than other groups. Copenhagen parents fell in between the other groups in measures of contact and care. St James-Roberts and colleagues found in this study that 'infant-demand' care reduced overall crying by a third at five to six weeks, but increased the number of infants who continued to wake and signal in the night at twelve weeks of age (St James-Roberts *et al*, 2006). The principal risk factor found in poor sleep patterns in this study was frequent feeding (>11 feeds per 24 hours) at one week of age (Nikolopoulou & St James Roberts, 2003).

Parents often attribute poor sleep behaviours to the difference between breast and bottle fed babies. Mothers who were breastfeeding at five months were more likely to have infants who were waking regularly at night than those who were bottle feeding (Wolke *et al*, 1995). Recent reports by mothers of infants that breastfed at six months of age suggested infants were sixty-six percent more likely to wake and signal during the night and seventy-two percent more likely to report difficulty sleeping alone but it was not associated with restless sleep or problems getting to sleep for the infant (Galbally *et al*, 2013).

Several RCT's have shown that providing parents with information on normal infant sleep/wake patterns and settling methods significantly improves sleep behaviour when compared with control group infants (Kerr *et al*, 1996; Symon *et al*, 2005; Wolfson *et al*, 1992). Wolfson and colleagues (1992) provided parents with two prenatal and two postnatal group sessions that taught parents about sleep and settling methods. They demonstrated better sleep patterns in the study group infants compared with the control group at one, two and three weeks of age (Wolfson *et al*, 1992). In another study, parents were randomly allocated to receive either a forty-five minute consultation with a nurse accompanied by written information at infant age three weeks or usual care (Symon *et al*, 2005). Symon *et al* (2005) found that the intervention infants were significantly more likely to have at least fifteen hours of sleep per twenty-four hours compared with control infants. The sample in this study was predominantly middle-upper class thereby limiting the generalisability of the findings. However, the data overall suggests an improvement in infant sleep behaviour when supportive information is provided to parents in the early stages.

Western parents are given conflicting advice about whether to introduce a 'scheduled' approach to infant care or to follow their infants' demands (St James-Roberts *et al*, 2006). The strongest and most reliable evidence is that behavioural modification methods can help parents manage crying and sleep problems (Nikolopoulou & St James-Roberts, 2003; St James-Roberts *et al*, 2001; Wolfson *et al*, 1992). A consistent approach in which the needs of the baby are addressed (e.g., irritable babies require a consistent approach to their sleep routine), as well as the needs of the parent, is important (Hiscock & Jordan, 2004). One example of a structured behaviour programme is described by Pinilla and Birch (1993), which consists of three main steps. First, parents are asked to maximise the difference between day and night time environments, by minimising light and social interaction at night. Second, they are asked to settle a baby judged to be sleepy in a cot or similar place, and to avoid feeding or cuddling to sleep, at night time. Third, once the baby is three weeks old, healthy, and putting on weight normally, they can begin to delay feeding when baby wakes at night, in order to dissociate waking from feeding. In a three-armed RCT, St James-Roberts *et al* (2001) demonstrated significantly more infants were sleeping through the night from the group who received this structured behavioural programme compared with control groups, by twelve weeks of age. The Pinilla & Birch (1993) approach has been successful in addressing sleep problems with eighty-two percent of the infants given the behavioural programme, compared to sixty-one percent of infants in the control group sleeping through the night (Nikolopoulou & St James Roberts, 2003). However, these programmes can be difficult to implement due to parental non-compliance and not all parents will regard having a baby who sleeps through the night by twelve weeks of age as a priority (St James-Roberts *et al*, 2001).

It has been suggested that infant temperament is unaffected by a behavioural approach to sleep patterns in babies under eight weeks of age (Pinilla & Birch, 1993). One proposal is that the neurological systems underlying voluntary behaviour remain immature in human babies until three months of age, placing limits on their regulatory capacities so that external attempts to shape their behaviour are less successful (Barr *et al*, 1992). This is supported by the findings of Van Ijzendoorn & Hubbard (2000), who reported that the time to respond to an infant's cries in the first nine weeks of life did not predict how much babies cried in later weeks. Another proposal is that parents are primarily concerned with their babies' well-being and growth at this age, so that they are less inclined to introduce constraints (St James-Roberts *et al*, 2001).

De Marcus *et al* (2015) suggest that the use of subjective measurements of sleep and temperament, and the paucity of longitudinal data, has resulted in inconsistent findings. They attempted to address this by objectively assessing infant sleep among ninety-five infants at three to twelve months of age with an actigraph in the home setting. A relationship was found, especially among girls, between both hyposensitive and hypersensitive infants and a risk of poor sleep quality. These are the first research findings suggesting that low reactivity in infancy might be associated with compromised sleep quality.

Although there is much research into the associations between infant sleeping problems and crying, there are still contradictory findings about the order in which they become evident, and the relationship to unsettled infant behaviour, with no conclusive data on the processes involved. Some of the strongest evidence indicates that sleep dysregulation is associated with poor sleep behaviour structures and that positive results are achieved when sleep behaviour programmes are implemented correctly and consistently.

4.3 Feeding difficulties

Factors such as underfeeding, overfeeding, swallowing excessive amounts of air, or not being adequately burped have been cited as contributing to infant unsettledness and colic (Carey, 1984). Parents who seek professional help for unexplained inconsolable crying also frequently report associated difficulties with infant feeding (Von Hofacker & Papousek, 1998). The need for regulation of feeding for an infant's overall development has been demonstrated (Dowling, 1977), therefore, it is important to identify early on if the unsettled behaviour is as a result of a feeding difficulty and should be managed accordingly. Chatoor (2002) suggested that infants who have difficulties reaching and maintaining a state of alert calmness, who are too sleepy, excited, or distressed to feed, are also at risk of a shortened duration of full breastfeeding or serious feeding problems, while others suggest a relative lack of association between feeding type and crying (Wolke *et al*, 1995).

In a small study by Miller-Loncar *et al* (2004), infants with persistent crying were more likely to have feeding difficulties and disorganised feeding patterns compared to settled 'non-colic' infants. However, a causal relation between colic and feeding problems from this study could not be determined. The possibility that feeding problems contribute to colic symptoms, or that colic contributes to feeding problems, or that they are co-occurring conditions with similar aetiologies was considered. It was also suggested that disorganised feeding patterns in infants with colic could indicate an underlying disorder in behavioural regulation (Miller-Loncar *et al*, 2004).

Douglas & Hiscock (2010) suggested an increased risk of breastfeeding cessation due to a failure to identify and correct breastfeeding problems. Changes from breast- to bottle-feeding are more often initiated by parents when infants cry excessively without clear causal pathways (Hide & Guyer, 1982). Clifford *et al* (2009) propose that breastfeeding does not have a protective effect on the development of colic; however, other researchers disagree. Using maternal reports, Cohen Engler *et al* (2012) demonstrated breastfed four to six month old infants had fewer crying episodes and less severe crying events. They suggested a potential role for melatonin, supplied to the infant via the breast milk during the night, in reducing colic symptoms in breastfed infants (Cohen Engler *et al,* 2012).

Changes in formula feed have frequently been recommended for crying problems and are adopted by parents with and without paediatric advice (Forsyth *et al*, 1985b). This may change the pattern of crying by small amounts in non-problem criers (Barr *et al*, 1989), but there is no evidence of its effectiveness in infants who cry excessively and have unsettled behaviour (Forsyth *et al*, 1985a). Therefore, changing from breast- to bottle-feeding, or changing the type of formula, is not recommended in the absence of diagnostic evidence (Forsyth *et al*, 1985a).

4.4 Chapter summary

Problems with self-regulation, including sleep, feeding, state control, self-calming, sensory reactivity, mood regulation, and emotional and behavioural control, have been documented during infancy (DeGangi *et al*, 2000). Suggestions of a relationship between these behaviours, often referred to as regulatory problems, have been explored. Early studies were retrospective, potentially exaggerating the relationships. Longitudinal analyses have found some distinct differences between excessive crying in infants and sleeping and feeding problems. Infant crying, and parental concern about it, peak at around five to six weeks of age, with the crying occurring mainly in the daytime and evenings (Barr, 1990b; St James-Roberts, 1989). Infant sleep-waking problems occur at night and after three months of age (Adams *et al*, 2004; Lozoff *et al*, 1985; Messer & Richards, 1993). Even when parents report that infants ‘sleep through the night’ by three months of age, infrared video recordings show that most babies continue to wake up in the night (Anders *et al*, 1992; Goodlin-Jones *et al*, 2001; Minde *et al*, 1993). The key distinction is not why infants awake, but rather why up to twenty-five percent of babies continue to 'signal' parents upon waking rather than resettling autonomously (Anders *et al*, 1992; Goodlin-Jones *et al,* 2001; Minde *et al*, 1993). Prospective relationships between infant crying in the first three months and night waking and signalling after six months of age are weak (St James-Roberts & Plewis, 1996; Wake *et al*,.2006; Wolke *et al*, 1995). Infants can exhibit problematic crying in early infancy or unsettled night-time behaviour after six months of age (von Kries *et al,* 2006; Wolke *et al*, 1995).

A relationship between feeding difficulties and unsettled infant behaviour is weak and evidence is contradictory. The involvement of feeding mechanisms with regulatory disorganisation has not been confirmed and the efficacy of making adjustments to routine feeding methods has not been proven. However, the reduction in symptoms associated with regulatory problems after altering parenting behaviour has been repeatedly reported (Kerwin, 1999; Ramchandan *et al,* 2000; Taubman, 1984; Wolke *et al*, 1994). In a systematic review, Hemmi *et al* (2001) reported that behavioural intervention programmes for regulatory disturbed children may promote a positive parent–child relationship and also positively influence behavioural development.

In chapter 5, the next chapter in the series on unsettled infant behaviour, environmental processes including pregnancy, birth, maternal mood and care-giving practices are discussed. Diagnostic issues, long-term effects, risk factors and management strategies of unsettled infant behaviour, and the view that early behavioural problems can be signals for ongoing toddler and childhood issues, are discussed in chapter 6, which is the final chapter in this series.

Chapter 5 - Parental influences on unsettled infant behaviour

Understanding the processes involved in early infancy, which cause one baby to be more unsettled than another has stimulated much debate. Yet, there is no conclusive evidence to support any prominent theory. There is paucity of research into whether discomfort of the musculoskeletal system in infants may play a role in unsettled infant behaviour. To carry out new research in this area, the broadness of the topic needs to be appreciated and addressed. This requires a wide review of the literature on unsettled infant behaviour but concentrating on topics of greatest relevance to the research question for this study, i.e. finding an association between unsettled infant behaviour and postural asymmetry in infants.

In the previous chapters on unsettled infant behaviour, the physiological, regulatory and behavioural systems within the infant have been explored. This chapter examines the external systems with which the infant interacts and are believed to play a role in the way an infant expresses behaviours. The effects of maternal physical and mental health in pregnancy, labour and post-partum are discussed, including medication and interventions. Mother-infant relationships are presented, with reference to different care-giving practices observed across a range of cultures. Given the weight of available evidence, the argument of whether these external factors can impact infant behaviour in a positive or negative way, is discussed. As expressed in previous chapters, the terms used by individual authors to refer to unsettled infant behaviour are maintained in this text.

5.1 Effects of pregnancy, labour and birth

Several factors in pregnancy, labour and during the birth of a baby have been linked with subsequent development of unsettled infant behaviour. The development of unsettled behaviour and infantile colic has been linked to maternal stress, musculoskeletal discomfort during the pregnancy (Hogdall *et al*, 1991; Rautava *et al*, 1993) and significant maternal medication during labour (Hogdall *et al*, 1991; Rautava *et al*, 1993), though these findings have not been consistently found (Murray *et al*, 1981; Thomas, 1981; Reijneveld *et al*, 2001). Maternal smoking during pregnancy and the lactation period have been associated with infantile colic (Matheson & Rivrud, 1989; Reijneveld *et al*, 2000; Said *et al*, 1984; Søndergaard *et al*; 2001). Studies on associations between birth weight and colic have been performed but results are inconsistent (Søndergaard *et al*, 2000).

Thomas (1981) suggested that the significant increase in reported infantile colic from that found in the 1960's was due to increased management, intervention and drug use during labour. This was said to reflect cultural changes in attitudes to childbirth, in particular, the increased usage of epidural block (Thomas, 1981). Thomas (1981) reported that forceps delivery and epidural anaesthesia were associated with subsequent development of colic. He also suggested that societies in which the approach to childbirth and labour was more relaxed, seldom had major problems in labour. He supported this by attributing the undocumented existence of infantile colic in Guatemala to the observation that ninety-eight percent of women in this society delivered their babies in the more natural kneeling or squatting position (Thomas 1981). Other researchers have shown that epidural block can result in foetal malposition (Hoult *et al*, 1977) and a twenty times increase in forceps delivery (Studd *et al*, 1980). There are contrasting reports about the effects of length of labour, with some researchers reporting a correlation between unsettled infant behaviour and a short second phase of birth (Vejsgaard Vestager *et al*, 2007; Wiberg & Nilsson, 2000) while Thomas (1981) associates prolonged labour with unsettled behaviour.

Hogdall *et al* (1991) found a link between some obstetrical procedures and a significantly increased risk of the baby being transferred to an intensive care unit and Hiscock & Jordan (2004) proposed a relationship between traumatic birth and subsequent infant discomfort and distress. Taddio *et al* (1994) examined the long-term effects of injury and tissue damage sustained in the neonatal period. In a prospective cohort study of eighty-seven healthy, full-term, male, newborn infants they demonstrated changes in central neural function persisting after tissue healing, and associated this with behavioural responses to pain months later (Taddio *et al*, 1994).

However, a study by Rao and colleagues (2004) did not find a relationship between obstetric history and infant behaviour. In a prospective long-term cohort study of over 400 babies, they found that obstetric complications such as gestational diabetes, hypertension, emergency caesarean section, premature rupture of membranes, placenta praevia, or obstructed labour, had no bearing on infant unsettledness (Rao *et al*, 2004). In the same study neonatal factors including birth trauma, resuscitation in the delivery room, admission to the neonatal intensive care units, presence of metabolic disturbances, and treatments for neurological or pulmonary disorders were not found to differ between normal and unsettled babies (Rao *et al*, 2004).

Although events in pregnancy and during the labour cannot be linked definitively with unsettled infant behaviour or colic, the weight of evidence would suggest that a causal pathway may exist. Elucidating specific processes in the ante- and peri-natal periods that could result in musculoskeletal discomfort, and consequent unsettledness of the infant, is important and this requires further investigation. Musculoskeletal disorders associated with asymmetry in young infants is explored in more detail in chapter 10.

5.2 Maternal mood

The inter-relationship between maternal mood and infantile behaviour is well documented. However, the cause and effect debate may be futile given the close bond between mothers and infants and how they influence each other (Papousek & von Hofacker, 1998). The incidence of infantile colic has been linked with psychosocial factors, systemic family problems and psychological factors of the mother including, stressful pregnancy, parental anxiety, maternal depression, dissatisfaction with sexual relationship and negative experiences during childbirth, as well as poor parental skills (Barr, 1998b; Canivet *et al*, 2005; Rautava *et al*, 1993; Reijneveld *et al*, 2001). Armstrong *et al* (2000) suggest that the quality of the parental relationship has an influence on perceptions of the infants' behaviour. Indeed, one large-scale study that assessed the impact of psychological, psychosocial and socioeconomic factors on the risk of having a child with infantile colic reported that not cohabiting with the child's father was the factor with the strongest association (Canivet *et al*, 2005).

Approximately ten percent of women suffer from depression in the first few months after birth (Cooper & Murray, 1998). A subsample of twenty-four women who had experienced pregnancy problems were more depressed and anxious postpartum and interacted less with their infants (Field *et al*, 1985). Infantile colic at two months of age has been associated with high maternal depression scores four to five months later (Barr *et al*, 1998, Vik *et al*, 2009). In a longitudinal study of middle income first-time mothers using self-report data, Fleming and colleagues (1988) revealed that pregnancy and postpartum mood states together explain a high proportion of the variance in mothers' maternal attitudes during the postpartum period. However, differences in maternal behaviour between depressed and non-depressed mothers during the early postpartum period were no longer apparent at sixteen months postpartum (Fleming *et al*, 1988).

The relationship between infantile colic and maternal depression has been found in many cross-sectional studies (Akman *et al*, 2006; Armstrong *et al*, 1998a; Armstrong *et al*, 2000; Barnett *et al*, 1993; Carey, 1968; Howell *et al*, 2006; McMahon *et al*, 2001; Milgrom *et al*, 1995; Miller *et al*, 1993; Miller-Loncar *et al*, 2004; Murray, 1997; Papousek & Papousek, 1990; Papousek & von Hofacker, 1998; Pauli-Pott *et al*, 2000; Wake *et al*, 2006) indicating the importance of the mother-child dyad. Yet the causal direction of these associations remains uncertain (McCallum *et al*, 2011; Miller *et al*, 1993). Armstrong and colleagues (1998a) described a ‘chicken and egg’ conundrum with respect to separating out the effects of infant crying, maternal mood and caretaking behaviours. For example, early problems with infant behaviour can affect the parents’ overall functioning, yet parents’ functioning (e.g., depression, stress) is likely to affect the child’s capacity to self-regulate and to develop healthy parent-child relationships (DeGangi *et al*, 2000).

Some suggest that it is important to assess the mother–infant relationship together with maternal fatigue, anxiety and depression (Chatoor, 2002, Hiscock & Jordan, 2004). The mother may be emotionally and physically unavailable to help her baby with the early stages of learning to self-soothe and anticipate comfort (Hiscock & Jordan, 2004). Postnatal depression may lead to flattened affect, with less animated mother-infant interactions and reduced responsiveness to the infant, leading to unsettled infant behaviour (Milgrom *et al*, 1995; Righetti-Veltema *et al*, 2002). In a recent study, Kohlhoffa *et al* (2015) highlighted the prevalence of Adult Separation Anxiety Disorder among first time mothers experiencing early parenting difficulties with unsettled infants. Spitz (1951) suggested an innate response in the baby to maternal anxiety. It seems that poor interactive experiences, with insensitive and unresponsive mothers, may cause the infant to express less positive emotionality (Belsky *et al*, 1991). It is important to address anxiety symptoms both with respect to the interventions offered to mothers and the potential impact on infant development (Mc Mahon *et al*, 2001; Oberklaid, 2000). This is supported further by findings that propose irritable newborns became less irritable with age if their mothers are responsive and calm (Fish *et al*, 1991; Van den Boom, 1994) and good patterns of mother–infant interaction are related to increases in an infant’s positive emotionality and activity level (Costa & Figueiredo, 2011).

Other evidence suggests that while low maternal mood may make it difficult to deal with an infant’s irritability or unresponsiveness, it has little effect on infant behaviour (Crcnec *et al*, 2010). Radesky *et al* (2013) observed that asking a mother about her ability to soothe her infant may be more relevant for potential intervention than questions about crying and fussing duration alone. This finding was replicated in cross-sectional studies completed in Canada (n = 1065) and the USA (n = 1857) in which Fujiwara *et al* (2011) reported that the length of individual unsoothable crying bouts was most strongly related to caregiver frustration when compared with overall daily duration and frequency of infant crying.

A review by Mayberry and Alfonso (1993) found an association between early infant temperament and postpartum depression. This was supported by a longitudinal study of 139 women from the third trimester of pregnancy through eight months postpartum, who completed depression scales at several time points and rated their infant's characteristics and childcare stress at two- and six-months postpartum (McGrath, 2007). Mothers' reports of infant temperament were significantly different for depressed and non-depressed mothers, with depressed mothers reporting more difficult infants at both measurement points (McGrath, 2007). These results suggest that maternal mood has an impact on mothers' perception of infant behaviour.

Another theory is that infant behaviour affects maternal mood. It is likely that unsettled infant behaviour reduces a woman's confidence in her ability to parent, and increases the likelihood that she will feel anxious, depressed and frustrated in her interactions with the baby (Armstrong *et al*, 1998a; Mayberry & Affonso, 1993; Murray & Cooper, 1997; Rowe & Fisher, 2010). As already discussed in chapter 4, a prominent non-disease explanation is that colic is an early clinical manifestation of a more reactive, less regulated temperament (Rothbart & Derryberry, 1981). Infants with such temperaments are expected to express more frequent and more intense negative affect, less soothability, and less predictability in responding; characteristics that often make them difficult for caregivers to manage (Rothbart, 1989). Difficult infant temperament might encumber the intuitive parental competence resulting in dysfunctional interactions (Wurmser *et al*, 2001).

Bruning and McMahon (2009) conducted a randomised controlled experimental trial to explore the impact of infant crying on mood, perceptions of temperament and caregiving behaviours in young women. They found an immediate impact on young women's negative affect, state anxiety and more negative perceptions of infant temperament. Data from 1015 mothers and their children participating in a prospective cross-sectional European multicentre study, by Vik and colleagues (2006), showed that infant crying was associated with high Edinburgh Postnatal Depression Scale (EPDS) (Cox *et al*, 1987) scores at two and six months postpartum. The literature is conflicting regarding long-term effects on maternal mental health, when the colic has resolved. Some studies reported that mothers of infants with colic felt less competent, tended to have more separation anxiety and that they reported more stress, compared with mothers of non-colic infants (Rautava *et al*, 1995; Stifter & Bono, 1998; Vik, 2009), whereas others did not find an increased risk of later depression once colic had resolved (Wake *et al*, 2006; Clifford *et al*, 2002). In a number of studies parents have reported that infants with colic have more difficult temperaments both during (Barr *et al*, 1992; Lester *et al*, 1992) and after (Carey, 1971, 1984; Lehtonen *et al*, 1994a; Papousek & von Hofacker, 1998; Weissbluth *et al*, 1984) colic has resolved, demonstrating the risk of parental perceptions when reporting on unsettled behaviour.

Lam *et al* (2003) found that infant sleep problems preceded rather than were a consequence of maternal depression (Fisher *et al*, 2009). This is supported by Crncec *et al* (2010) who argue against focussing solely on treatment of a mother's depression, particularly for sleep disturbance and other research suggesting robust improvements to maternal mood following successful sleep disturbance treatment (Mc Mahon *et al*, 2001; Schmid *et al*, 2010). Undoubtedly there is a close association between maternal mood and reported unsettled infant behaviour but more research is required to clarify the cause and effect relationship. It is quite feasible that a mutually dependent situation exists between these two conditions, with one exacerbating the other until the pattern of behaviour between mother and infant is managed. To have the greatest effect, intervention to address mother-infant interactions should be considered as early as when the mother is preparing for her transition to parenthood.

5.3 Transition to parenthood

The transition to parenthood is a time of significant physical, emotional, and psychological change for families. Lack of preparedness of motherhood has been identified as an issue for many mothers. Rubin (1984 as cited in George, 2005) described a fourth trimester of pregnancy as a significant period of transition and recovery. Rubin states that becoming a mother is a process of learned behaviour; this time immediately following childbirth and extending into the weeks and months following is an important period in the process of development for new mothers. George (2005) conducted in-depth interviews with participants guided by open-ended semi-structured questions and using qualitative, grounded theory and identified that following the dramatic changes of pregnancy and delivery, the women in this study returned home feeling unprepared to care for themselves and their babies. Because of their lack of preparedness at a time of increased responsibility and vulnerability, they were overwhelmed. The sense of abandonment by the healthcare system was also a significant component of the experiences of the new mothers in this study (George, 2005).

According to Rao *et al* (2004) first born infants are more likely to develop infantile colic than subsequent siblings. Earlier reports support this finding (Leung *et al*, 1997; Miller *et al*, 1989; Stahlberg 1984) including a prospective study of 130 infants using a parent-report questionnaire (Thomas, 1981). Carey (1968) and St James-Roberts and Halil (1991) suggest that first and later-born infants cry the same amount, but parents are more likely to take their first-borns to the clinician with crying concerns.

In a meta-synthesis development of nine qualitative studies relating to the transition to motherhood, Nelson (2003) reported that to facilitate maternal transition, nurses must remain sensitive to the maternal insecurity of primiparae and encourage their maximum maternal engagement. This is particularly important during periods of forced mother-infant separation, such as the newborn's admission to the intensive-care unit (Nelson, 2003). For women to feel comfortable caring for their infants, they have to master skills and come to know their individual child, which can take first time mothers at least three months (Sethi, 1995). In addition, prenatal discussion of realistic expectations for the transitional period, ongoing support through the first six months postpartum, and the use of role models should be integrated into postpartum support programmes, to assist mothers in negotiating typical areas of disruption during maternal transition.

5.4 Different care giving practices

Parental care-giving practices are thought to be acquired in the context of the values and practices of extended families and of community and cultural attitudes, beliefs and norms relating to appropriate parenting and feeding methods (Fisher *et al*, 2009). Different care-giving practices may influence the total daily duration of crying in very early infancy (Fisher *et al*, 2009; St James-Roberts *et al*, 2006). Some observations suggest that infantile colic may result, in part, from an inadvertent failure of the parents to respond appropriately to baby cues (Leung *et al*, 1997; Taubman, 1984).

The anthropological term 'proximal care' refers to prolonged holding, frequent breastfeeding, rapid response to infant cries and co-sleeping with infants at night (Hewlett *et al*, 1998). Research has shown that proximal care in Africa (Barr *et al*, 1991; Hewlett *et al*, 1998), India (St James-Roberts *et al*, 1994), Korea (Lee, 1994) and Copenhagen (Alvarez, 2004) are associated with lower amounts of overall fussing and crying than are typical in London and North American infants (St James-Roberts, 2001; Hunziker & Barr, 1986; Brazelton, 1962). None of these data were confirmed with tape or video recordings and, therefore, might reflect different reporting styles rather than absolute differences in crying duration; studies have shown that parents typically report approximately four to five times more crying than tape recordings (Barr *et al*, 1988; St. James-Roberts *et al*, 1996). However, proximal care was also associated with increased waking and crying at night at twelve weeks of age (St James-Roberts *et al*, 2006) and some studies suggest that increased carrying made no difference when infants were already crying a lot (Forsyth *et al*, 1985b; St James-Roberts *et al*, 1995; Walker & Menaheim, 1994).

Therefore, the debate about best care-giving practices has persisted with different associated benefits and costs.

Early studies reported an association between maternal intelligence and education and development of colic in their infants, possibly because of better reporting or lower maternal tolerance (Boulton & Rowley, 1979; Paradise, 1966). Yet, Wurmser *et al* (2001) found no relationship between abnormal crying during or beyond the first three months of postnatal life with respect to sex, residence, birth order, duration of parental school education, maternal age and feeding mode. It should be noted that the data in this study was collected several months after the crying had settled and thus may be subject to recall bias. Gartstein & Rothbart (2003) recommend a maximum interval of one to two weeks for reliable recall of infant behaviour, particularly when parental reports of infant crying have been found to be exaggerated (Barr *et al*, 1988; St. James-Roberts *et al*, 1996).

With the emergence in the field of complexity science some research into unsettledness in infants, and how it relates to maternal mood, is undergoing a paradigm shift, from a reductionist to a systemic or holistic approach (Douglas & Hiscock, 2010). In complexity science, a complex adaptive system (CAS) is a dynamic network of systems acting in parallel, yet interconnected and interacting. Douglas *et al* (2011) refers to the mother-baby CAS – suggesting that all the emerging problems of the mother and baby relationship through pregnancy, inter-partum, post-partum and beyond, is encapsulated within a system and is not affected by external stimuli. Therefore, a mother-baby CAS is made up of multiple known and unknown dynamically interacting and co-evolving factors out of which cry-fuss behaviours emerge, and demands a transdisciplinary integration of evidence. Understanding the sensitivity to initial conditions that operate in the mother-baby CAS can help to make sense of the complicated inter-relationships between failure to thrive, aversive feeding behaviours and unsettledness and prevents the inappropriate diagnosis of other conditions (Douglas & Hiscock, 2010). Bowlby (1982) recognised the contribution of the infant to developing mother-infant attachment. He hypothesized that basic infant behaviour such as sucking, crying, and smiling act as stimuli that induce the mother to respond. The pattern of her responses shapes the infant's behavioural systems into an integrated response (Bowlby, 1982).

Close body contact (skin-to-skin) immediately after birth between mother and baby seems to regulate the newborn's temperature, energy conservation, and acid–base balance, along with adjustment of respiration, crying, and nursing behaviours (Winberg, 2005). This is supported by the work of Feldman *et al* (2002) on pre-term babies in neonatal intensive care units who reported that mother-infant skin-to-skin care, also referred to as kangaroo care, had a significant positive impact on the infant's perceptual-cognitive and motor development and on the parenting process. They speculated that kangaroo care had both a direct impact on infant development by contributing to neurophysiological organisation, and an indirect effect by improving parental mood, perceptions, and interactive behaviour. During the following few months of life, the foundation for the regulation of feeding, sleep, and emotions is laid (Chatoor, 2002).

The evidence would suggest that the mother-infant relationship plays an important role in infant behaviour, particularly when it comes to reading and responding to baby signals, confidence in care-giving practices and post-natal mental health. It is also recognised that the relationship is two-way and the mother's parenting skills and confidence can be jeopardised by unsettled behaviour in early infancy. Re-framing the mother and baby as a CAS emphasises the importance of early intervention from the first days and weeks by a co-ordinated multidisciplinary team, and emphasises the importance of supporting parents' trust in their baby's innate capacity for self-regulation in the first few months of life (Douglas *et al*, 2011).

5.5 Chapter summary

Much of the literature emphasises the negative impact that maternal behaviour, mood and parenting styles can have on the psychosocial development of infants. This includes pregnancy health, transition to motherhood and post-natal depression, and places much of the responsibility of infant behaviour and unsettledness with the mother. It is important to acknowledge that the direction of effect is reciprocal, with a crying baby also negatively influencing the mother (Miller *et al*, 1993). Consequently health professionals can assess the difficulty the mother may be experiencing in caring for an inconsolable infant and provide reassurance, support and understanding of her situation. As many babies cry a lot in the first three months of life, even with excellent parental care (St James-Roberts, 2001), it is also important for first time parents to receive information about developmentally normal crying behaviour (Bruning & McMahon, 2009) and instruction on effectively reading baby cues.

Chapter 6, the final chapter in the Unsettled Infant Behaviour series, describes the diagnostic issues, long-term effects, risk factors and management strategies associated with unsettled infant behaviour.

Chapter 6 - Long-term risks and management of unsettled infant behaviour

In view of the challenges presented in earlier chapters when investigating the cause and effects of unsettled infant behaviour, this chapter addresses the problems specific to diagnosis and management. What is clear from the research is that unsettled behaviour in infancy, whether it is referred to as infantile colic, difficult temperament, or regulatory problems, is a cause of significant disturbance within families and increased demands on medical services. Yet the theories underpinning the nature of the disorder are disputed and there is diagnostic uncertainty, which in part, may reflect the variety of existing theories. Suggested treatment protocols also vary with no one approach offering a clear benefit over others. The long-term effects of misdiagnosis, late intervention and inappropriate management is also addressed in this chapter with particular focus on the concerning risk of infant abuse associated with unsettled infant behaviour.

6.1 Diagnosis of unsettled infant behaviour

Reliable diagnosis and correct management of unsettled infant behaviour is limited by the complexity of the underlying issues and a lack of cross-professional consensus (Douglas *et al*, 2012). As a systematic approach to diagnosis is lacking; identifying which infantile condition may be causing the unsettled behaviour is problematic due to the common presentation of associated symptoms. This may lead to misdiagnosis, which results in incorrect management protocols that could be harmful. The situation is further complicated by inconsistencies in language and definitions, and unreliable diagnostic testing protocols leading to a reliance on clinical judgement. Thus, management of unsettled infant behaviour can be challenging in primary healthcare.

Assessing pain in young infants is difficult because they lack the verbal ability to communicate the location and severity of pain (Fuller, 2001). There is an absence of reliable and valid clinical tools for diagnosis of pain conditions in infants. Due to the mixed theories about aetiology, and the complexity and variability of the presentations, there are problems formulating a reliable diagnosis. Assumptions are often made about the underlying cause and many infants are diagnosed as having a medical problem, including gastro-oesophageal reflux disease (GORD), cow's milk protein allergy (CMPA), lactose intolerance and gut irritability (Armstrong *et al*, 1994). Attempts to address these problems can lead to changing the infant's food or the mothers' diet, as well as medication in some cases. Medication usage seems to be based more on an aetiological theory of 'excess irritability' than on any plausible science (Thomas, 1995) leading to the inappropriate diagnoses and/or medication use in these infants (Armstrong *et al*, 2000). Families often complain that they receive conflicting advice from health professionals about how to manage the unsettled behaviour. This indicates that unsettled behaviour in infants is a complex problem and a simplistic, biomedical approach may be harmful if the incorrect diagnosis is made (Douglas *et al*, 2011).

Substantial discrepancies between recordings of infant crying and parental records (Barr *et al*, 1988; St. James-Roberts *et al*, 1996) provide an example of the importance of definition and method. The literature on infant crying reports different data for the amount of time infants cry, and studies that show reduced crying after changes in parental care cannot be replicated in subsequent research (Hunziker & Barr 1986; Nikolopoulou & St James-Roberts, 2003; Pinilla & Birch, 1993; St James-Roberts *et al*, 2001; Taubman, 1988; Wolfson *et al*, 1992). Until a consensus is reached on what should be measured when examining unsettled infant behaviour, and appropriate measurement tools, agreement between different studies will be difficult to achieve.

6.2 Long-term effects

It is important to explore the extent to which unsettled infant behaviour predicts continuing temperamental difficulty and toddler behaviour problems (Mc Mahon *et al*, 2001). Longitudinal studies suggest that parents of colicky infants still report more family distress three years later (Agresti, 1990; Lehtonen *et al*, 1994a; Rautava *et al*, 1995). Stifter & Bono (1998) examined mothers eighteen months after birth and found that mothers of infants with colic felt less competent as mothers, and tended to have more separation anxiety than mothers of non-colic infants. Families with a previous colicky infant were more likely to complain about a breakdown in caregiving roles (Papousek & Papousek, 1990; Papousek & von Hofacker, 1995) and family functioning (Lehtonen *et al*, 1994a; Rautava *et al*, 1993; Rautava *et al*, 1995; Barr, 1995) up to three years later. However, some report that transient regulatory problems, most notably excessive crying within the first three months, have an overall good prognosis without any negative long-term consequences in behaviour (Sloman *et al*, 1990; Stifter & Braungart , 1992; St James-Roberts *et al*, 1998; Wake *et al*, 2006), whereas persistent and/or multiple regulatory problems have been reported to affect the child's behaviour long term (DeGangi *et al*, 1993; DeGangi *et al*, 2000; DeSantis *et al*, 2004; Scher *et al*, 2005; Schmid *et al*, 2009; Wolke *et al*, 2002).

To explain the association between regulatory problems and behavioural problems later in childhood, some aetiological models suggest that hypersensitivity to stimuli (DeSantis *et al*, 2004), ineffective regulatory competences (Olson *et al*, 2002) or early deficit in executive control (Wolke *et al*, 2002; DeGangi *et al*, 1993) may be precursors of less effective regulation of behaviour (Wolke *et al*, 1995). Many researchers have speculated that persistent problems with behavioural control, such as inability to stop crying and to regulate sleeping and feeding behaviour in infancy, are the prodromal stage of behaviour control difficulties, such as hyperactivity and lower intelligence scores in childhood (DeGangi *et al*, 1991; Moffitt *et al*, 1996; Rao *et al*, 2004; Sanson *et al*, 1998; von Kries *et al*, 2006; Wolke *et al*, 1995; Wolke *et al*, 2002). The systematic review of Hemmi *et al* (2011) found strong associations between regulatory problems and later internalising (anxiety, depression or withdrawal), externalising (aggressive or destructive behaviour, conduct problems or temper tantrums) and attention deficit hyperactivity disorder (ADHD) problems, and suggested that children with persistent regulatory problems in families with other challenges may require early interventions to minimise or prevent the long-term consequences of infant regulatory problems (Hemmi *et al*, 2011).

Parental perceptions that an infant is more difficult than average have been shown to be a strong predictor of later child behaviour problems in longitudinal research (Lehtonen *et al*, 2000; Sanson *et al*, 1991). Canivet *et al* (1996) followed up fifty formerly colicky infants and 102 controls at four years of age and found ex-colicky children displayed more negative emotions according to their temperament scale, though it could be argued that the time delay was too long for accurate parental recall in this study. DeGangi *et al* (2000) found that children initially diagnosed with moderate-to-severe regulatory disorders, reported through parental questionnaires, were at high risk for later perceptual, language, sensory integrative, and emotional/behavioural difficulties in the preschool years, even though the regulatory-disordered sample did not differ from their normal counterparts in developmental parameters during infancy. Caution also needs to be applied to these findings due to the small sample sizes in this study (DeGangi *et al*, 2000).

In contrast to the above findings, a recent study by Milidou and colleagues (2015) followed 27,940 children from the Danish National Birth Cohort (1997-2002), including 1879 (6.8%) with a history of infantile colic as defined according to the modified Wessel criteria. No evidence of a strong association between infantile colic and motor impairment and coordination difficulties later in life was found in this cohort (Milidou *et al*, 2015). Therefore, it cannot be concluded from the extant research that unsettled infant behaviour, or infantile colic, are necessary precursors to later developmental coordination problems. However, when present in combination with systemic family problems there does appear to be a relationship with long-term behavioural and emotional development, particularly if the regulatory problems are severe and last more than three months (Milidou *et al*, 2015).

6.3 Risk factors and abuse

While apparently innocuous, unsettled infant behaviour can prompt lasting parental distress (Canivet *et al*, 2000; Forsyth *et al*, 1985b; Miller *et al*, 1993; Rautava *et al*, 1995; Thompson *et al*, 1986). Disregarding unsettled behaviour as a transient developmental phenomenon, and thus failing to diagnose a treatable issue, risks entrenching maternal anxiety (Douglas & Hiscock, 2010). Although unsettled infant behaviour has been linked with substantial maternal mental health morbidity and disability (Fisher *et al*, 2009), exposure to excessive infant crying also appears to be associated with increased irritability in fathers towards the baby (Ellett *et al*, 2009). Irritability and crying are recognised as the chief complaints of infants who have had repetitive and violent shaking (Ludwig, 1984; Singer & Rosenberg, 1992). The natural peak of infant crying behaviour coincides with a peak age for severe infant injury or death as a result of child abuse (Overpeck *et al*, 1998). In infants aged six months, nearly six percent of parents reported taking at least one action to stop infant crying that might lead to child abuse (i.e., smothering, slapping, or shaking) and of whom one in five had taken more than one of these three actions (Reijineveld *et al*, 2004). Non-accidental injury should be considered in the child with excessive crying and with bone or soft tissue injuries on examination (O'Neill *et al*, 2014). Fractures occur in up to twenty-five percent of physically abused children and eighty percent of these fractures occur in children under eighteen months of age (O'Neill *et al*, 2014).

The potential severity of an episode of colic is highlighted by the fact that, for certain individuals, the stress of caring for an inconsolable infant may trigger physical abuse, such as that seen in Shaken Baby Syndrome (Levitzky & Cooper, 2000; Singer & Rosenberg, 1992). In many cases of Shaken Baby Syndrome, crying is often mentioned as a precipitant (Dykes, 1986; Levitt *et al*, 1996; Ludwig, 1984; Reijneveld *et al*, 2004) though these are usually based on anecdotal reports. It is noted that the age-specific incidence curve in hospitalized Shaken Baby Syndrome cases has a similar starting point and a similar shape to the normal crying curve, which serves as indirect evidence convergent with reports that early crying is a likely stimulus for Shaken Baby Syndrome, though there is high reliance on face validity. Abusive head trauma is the leading cause of death from traumatic brain injury in infants under two years (Koe *et al*, 2010). Consistent with early clustering of all forms of 'battering' in the first five months of life (Agran *et al*, 2003), crying may have wider significance as a stimulus for other forms of abuse as well. Persistent unsettled infant behaviours could exert an adverse effect on the quality of interactions, capacity for mutuality and shared approach to problem solving between partners, and there is a need for effective early interventions to include both parents (Fisher *et al*, 2009). This emphasises the importance of not focusing on the management of unsettled infant behaviour as a simplistic, biomedical problem and is consistent with evidence demonstrating the benefits of a multidisciplinary approach to include cross-professional collaboration and shared assessment frameworks for Primary Care Practitioners in maternity care (Douglas *et al*, 2012; Martin & Kasperski, 2010).

6.4 Management

The difficulty with management of unsettled infant behaviour is that often parents will try multiple different approaches, practitioners and methods to resolve the issues (Don *et al*, 2002). Without a clear aetiology for unsettled infant behaviour, there is no proven effective treatment. Information is available from self-help books, DVDs and websites and it might be difficult for parents to gauge the quality and reliability of this information, particularly regarding safety and risk (Fisher *et* *al*, 2009). Advice from family and friends can also be inconsistent, thus making the situation confusing and frustrating for parents.

An association between type of infant feeding and colic has not been found (Rao, 2004; Rautava *et al*, 1993) though breast-feeding to comfort infant crying is rated as a highly effective calming method by parents (Howard *et al*, 2006). There is little evidence to support changing infant food to help alleviate the symptoms of infantile colic (Leung, 1998; Wade & Kilgour, 2001) and although there is evidence of benefit from anti-colic medications (Lucassen *et al*, 1998) including simethicone (Wade & Kilgour, 2001; Danielsson & Hwang, 1985; Metcalf *et al*, 1994) there is a risk of adverse consequences. The use of dicyclomine hydrochloride for the treatment of infantile colic is contraindicated in infants under six months of age due to reports of serious side effects (Leung *et al*, 1997; Balon, 1997; Parkin *et al*, 1993) including drowsiness and constipation in five percent of cases (Lucassen *et al*, 1998). The administration of probiotics, such as *Lactobacillus reuteri* DSM 17938, have recently being proposed to reduce daily crying and fussing time (Chau *et al*, 2015; Savino *et al*, 2010; Sung *et al*, 2014; Szajewska *et al*, 2013) but the evidence is preliminary.

Evidence for the benefits from some complementary and alternative medicine (CAM) therapies (e.g. osteopathy, chiropractic, acupuncture and aromatherapy) is anecdotal and has not been supported by research (Olafsdottir *et al*, 2001; Skjeie *et al*, 2013), despite the fact that in Europe fifty-two percent of parents seek CAM therapy for their children (Zuzak *et al*, 2013). Olafsdottir *et al* (2001) in a randomised, blinded, placebo controlled trial could not demonstrate a benefit of chiropractic spinal manipulation over placebo in the treatment of infantile colic. Notwithstanding the paucity of evidence of the effectiveness of chiropractic (Ernst, 2012), neither is there evidence of its ineffectiveness (Olafsdottir *et al*, 2001; Wiberg *et al*, 1999) and many parents consult chiropractors for help managing infantile colic (Underwood, 2009). A review by Hughes and Bolton (2002) suggests that while chiropractic has no benefit over placebo in the treatment of infantile colic, there is evidence that taking a colicky infant to a chiropractor may result in fewer reported hours of colic by the parents. A plausible theoretical model for any possible benefit from consulting a chiropractor for infantile colic would include the more non-specific effects of reassurance and advice from a health professional, familiar with the problem and who has confidence that their treatment is effective (Underwood, 2009).

Studies showing benefits for CAM interventions were mostly of low methodological quality (Alcantara *et al*, 2011; Pizzolorusso *et al*, 2011). A prospective study by Pizzolorusso *et al* (2011) on the effect of osteopathic manipulative treatment in a sample of 350 consecutive premature infants admitted to a neonatal intensive care unit (NICU) showed a reduction in the occurrence of gastrointestinal symptoms and length of stay in the NICU, but there was no control group in this study. Dobson *et al* (2012) conducted a meta-analysis on manual therapies for infantile colic and found that studies were generally small and methodologically prone to bias, making it difficult to arrive at a definitive conclusion about the effectiveness of manipulative therapies for infantile colic, as well as the safety of these interventions.

There is relatively strong evidence of benefits from infant behaviour programmes, which include educating parents on normal crying and sleeping patterns, helping parents recognise baby cues and establishing a regular approach to response. A reduction in regulatory problem symptoms after altering parenting behaviour has been repeatedly reported (Kerwin, 1999; Ramchandan *et al*, 2000; Taubman, 1984; Wolke *et al*, 1994). The implementation of these programmes was found to improve infant behaviour (Don *et al*, 2002) and increased the number of infants who slept through the night by twelve weeks of age (Kerr *et al*, 1996; Nikolopoulou & St James-Roberts, 2003; Symon *et al*, 2005; Wolfson *et al*, 1992). Hemmi *et al* (2011) suggested the need for early intervention for prevention of regulatory problems. Behavioural intervention programmes for regulatory disturbed children may promote a positive parent–child relationship and also positively influence behavioural development. But compliance to such programmes can be difficult to control and other researchers found that behavioural programmes do not influence crying duration (St James-Roberts *et al*, 2001), prevent sleep and behavioural problems in later childhood, or protect against postnatal depression (Douglas & Hill, 2013).

Although there is no evidence on the cost effectiveness of behavioural intervention programmes (Morris *et al*, 2001), the early identification of vulnerable groups is important. Special attention is needed in terms of offering information and support in the maternal healthcare system to very young women, women who do not cohabit with the father, and women with high trait anxiety (Canivet *et al*, 2005). Given the prevalence and significance of cry-fuss behaviours in infants, and the economic burden of late, tertiary intervention, the design and evaluation of an integrated, evidence-based, multidisciplinary primary care approach to management of unsettled babies and their mothers, is a priority (Douglas & Hiscock, 2010; Douglas *et al*, 2011).

6.5 Chapter summary

Excessive, inconsolable infant crying and resistance to comforting have been associated with earlier cessation of breastfeeding, frequent changes of infant milk formula, maternal irritability, disrupted mother-infant relationship and heightened risk of infant abuse (Lehtonen *et al*, 2000; Wolke *et al*, 1994). Supporting the parents and correctly diagnosing and managing unsettled infant behaviour is an important process but one that is limited by the complexity of the underlying issues and a lack of consensus on diagnosis and management (Douglas *et al*, 2012). In addition, this condition is burdened by limitations in research methodologies. Diagnostic accuracy and efficacy of treatment protocols often rely on parental reporting. Many factors may lead to a risk of bias with this method of data collection style, not least parental perception, poor recall and the absence of blinding in the majority of studies. A lack of consistency in terminology, definitions and categorisations of infant behaviours further limits the possibility of reaching valid conclusions. There is general agreement on when infant crying becomes problematic, mostly by using the Wessel 'rule of three's' criteria for infantile colic. But a primary issue is achieving a cross-professional agreement on how to examine, diagnose and manage these infants, and their families. Fundamental to this problem is the lack of understanding on causal processes and diagnostic strategies. Therefore, there is scope to investigate alternative clinical diagnostic features and indeed a need for better interventions in order to appropriately manage this distressing condition.

Chapter 7 – Infant Temperament Measurement

Interest in the measurement of infant behaviour, also referred to as infant temperament measurement, has increased steadily since the 1950's. During this time developing techniques for assessment has become an important area of study, with a variety of laboratory and parent-report questionnaire approaches now accessible (e.g., Brazelton, 1973; Carey & McDevitt, 1978; Gartstein & Rothbart, 2003; Rothbart, 1981; Thomas *et al*, 1963). When measuring difficult temperament in infants it is often associated 'by definition' with infantile colic because crying and fussing are predominant behaviours for both conditions (White *et al*, 2000). Establishing the relationship between difficult temperament and colic can be problematic, with some proposing that colic is an early manifestation of more reactive, less regulated temperament (White *et al*, 2000). Compelling evidence for the role of temperament in colic syndromes requires measures that have high construct validity and high discriminant validity with respect to crying and fussing (White *et al*, 2000). Likewise, although sleep patterns and temperament in the first year of life are closely related, research utilising objective rather than subjective measurements of sleep and temperament is scarce and results are inconsistent (DeMarcas *et al*, 2015). In order to better understand infant temperament and how it develops, is expressed and can be measured, this chapter explores this concept independent of its relationship to other childhood problems.

The use of maternal reports and infant diaries dominate research methodology primarily because recording infants' crying patterns reliably requires methods, which can measure during the day and night-time over several days. This is required to understand maternal perceptions of infant crying as well as to understanding the crying itself (St James-Roberts & Halil, 1991). The experiences of parents, the environments they live in and the interactions with their infants affect their perceptions of infant temperament (Carey & McDevitt, 1978; Persson-Blennow & McNeil, 1979; Rothbart, 1981). Different temperament assessment tools are presented, illustrating the development of infant temperament research over the past forty years. Rothbarts' Infant Behavior Questionnaire (IBQ) (Rothbart, 1981) and the revised version (Gartstein & Rothbart, 2003) are introduced in this chapter and further elucidated in chapter 8.

7.1 Infant temperament

Temperament has been described as the constellation of inborn traits that determines a child's unique behavioural style and the way he or she experiences and reacts to the world (Rothbart & Bates, 2006). That is, temperament refers to individual differences in reactivity and self-regulation that are present from birth and, at least to some extent, are biologically based (Buss & Plomin, 1984; Rothbart, 1986). Nine dimensions of infant temperament have been identified in comprehensive interview and observation rating studies of large samples of infants: motor activity; regularity of sleeping and feeding patterns; response to unfamiliar people or stimuli; ease of adaptation to change; intensity of emotional reactions; threshold to reaction; overall mood; distractibility; and persistence (Oberklaid *et al*, 1984; Sanson *et al*, 1985). Specifically, temperament in infancy refers to early differences in motor activity, smile-proneness, soothability, attention span, anger-proneness and fearful distress (Goldsmith & Rothbart, 1991).

Infants are born with distinguishable variation in temperament (Thomas *et al*, 1968), which exert significant affects on their interactions with the environment; especially care-givers (Hiscock & Jordon, 2004; Oberklaid *et al*, 1984). Thomas *et al* (1968) (as cited in Costa & Figueiredo, 2011) claim that at as early as the age of two or three months there is a discernible behavioural profile or temperament: 'easy', 'difficult', and 'slow to warm up'. The 'easy' children are characterised by a positive mood, regularity, low/moderate intensity of reaction, adaptability and approach. The 'slow to warm up' show a low activity level, only withdraw at the first exposure to stimuli, are slow to adapt, have a mildly negative mood and low intensity reactions. The 'difficult' children have irregular behaviour, intense reactions, withdraw from stimuli, have trouble adapting and a negative mood (Costa & Figueiredo, 2011). Accordingly, withdrawn infants have difficulties in engaging in new activities, approaching and giving vocal feedback compared to other infants. The most commonly researched temperament is 'difficult temperament' (Bates, 1983).

Early researchers viewed temperament as a continuum along an easy–difficult continuum (Thomas *et al*, 1963) and frequently considered a restricted set of dimensions, such as emotionality, activity, and sociability (e.g. Buss & Plomin, 1984). Constructs were assessed with considerable conceptual overlap, using scales with limited internal consistency (e.g., Carey & McDevitt, 1978; Rothbart & Mauro, 1990). More recently, research on infant temperament has evolved substantially leading to wide acceptance of the importance of temperament (Zentner & Shiner, 2012) which has emphasised aspects of regulation and recommended decomposition of broad traits, such as emotionality, into more distinctive elements, such as susceptibility to different negative emotions and differing levels of stimulation required to elicit positive affect (Putnam *et al*, 2014). As a result a broader multidimensional conceptualisation has emerged to include approach/withdrawal, inhibition, attention, activity, distress, and soothability (Molfese *et al*, 2011). In addition, three higher order factors have been identified by many researchers that underlie infant temperament; i.e. Orienting/Alertness, Negative Emotionality, and Surgency-Extraversion (Casalina *et al*, 2012; DeSantis *et al*, 2011; Gartstein *et al*, 2005; Gartstein & Rothbart, 2003; Putnam *et al*, 2006).

7.2 Parental perceptions of infant temperament

Parental recording has commonly been used to describe emerging patterns of infant behaviour with a potential for use in the clinical assessment of behavioural problems (Barr *et al*, 1988). However, the relationship between infant crying and parent rating of infant temperament is complex as the response relies heavily on the perceptions of parents and carers (Carey & McDevitt, 1978; Persson-Blennow & McNeil, 1979; Rothbart, 1981) whose circumstances, environments, handling methods, biases, recall ability and support networks can vary greatly and influence the overall experience. Difficult infant temperament and other infantile or parental factors (pre-, peri-, postnatal biological and psychosocial risks, child care attitude and psychological condition) might encumber the intuitive parental competence resulting in dysfunctional interactions (Wurmser *et al*, 2001).

According to Bates (1983), because difficult temperament is strongly related to parental perception and social interpretation of the child's behaviour it should be named perceived difficult temperament. Maternal characteristics including prenatal stress, anxiety, and personality structure, appear to influence maternal perception of infant temperament (McGrath *et al*, 2008). It is possible that parents' own characteristics are determinant in their views of their children's temperament related behaviour. However, it is also important to note that temperamentally different children may have a unique impact on parents' own personality traits, and in this sense, the influences are reciprocal (Macedo *et al*, 2011). Maternal reports on twenty-seven different scales were analysed and evidence was found to support the model that parent perceptions of children refer to both objective characteristics of the child and subjective characteristics of the parent (Bates & Bayles, 1984). Other researchers have demonstrated moderate associations between parental and observer ratings (Rothbart *et al*, 2001). Studies have found the number of minutes of tape-recorded crying is about twenty to twenty-five percent of the amount parents' record in behaviour diaries (Barr *et al*, 1988; St James-Roberts *et al*, 1996). Most challenging is that parents have been shown to continue, inaccurately, to perceive infants with colic as crying or reacting more to stimulation after the colic symptoms have subsided (Wolke *et al*, 1995) indicating the risk of confirmation bias as a result of the experience of living with an infant who had colic (White *et al*, 2000).

Recruitment of parents to participate in behaviour measurement studies can be problematic as this is already a demanding time (St James-Roberts *et al*, 2006). Successful recruitment is as low as twenty-five percent and parental participants are often mature, well educated, and in a stable relationship (Barr *et al*, 1988; Hunziker & Barr, 1986; St James-Roberts *et al*, 1995), which may bias results. Although the value of parent-report questionnaires is recognised in the study of infant behaviour, and for many reasons is regarded as the most reliable approach to data collection, the limitations of this methodology, particularly in terms of recruitment and parental perceptions, need to be considered in the interpretation of findings.

7.3 Development of temperament measurement

A number of prominent theories dominate research concerning the developmental origins and dimensions underlying temperamental features (Casalina *et al,* 2011). Since the 1950s a consistent association has been found between temperament and children's health and development. There are a number a different temperament measurement tools, which have been developed by researchers and changed with the emergence of new knowledge. The course of this development can be observed by examining the strengths and weaknesses of earlier models used in research since the introduction of the New York Longitudinal Study (Thomas *et al,* 1963). These include the Infant Temperament Questionnaire (Carey & McDevitt, 1978), the Early Infant Temperament Questionnaire (Medoff-Cooper *et al,* 1993), the Neonatal Behavioral Assessment Scale (Brazelton, 1973), the Alarm Distress Baby Scale (Guedeney & Fermanian, 2001), the Infant–Toddler Symptom Checklist (DeGangi *et al*, 1995), the Crying Patterns Questionnaire (St James-Roberts, 1988), the Barr chart (Barr *et al*, 1988) and the Infant Behavior Questionnaire (IBQ; Rothbart, 1981).

The New York Longitudinal Study (NYLS), started in 1956 and continued over several decades thereafter, is regarded as a classic study into personality types and temperament traits. The NYLS investigated the role of infant temperament in development (Thomas *et al,* 1963). They defined temperament as behavioural style, i.e. the how rather than the what or the why of behaviour. They assumed that parents can be used as an effective source of information about their children (Persson-Blennow & McNeil, 1979) and used direct observation and interviews with parents about their children. The NYLS identified nine temperament characteristics or traits and by observing a child's responses to everyday situations, the researchers could assess these temperaments. The researchers suggested that these nine traits were present at birth and continued to influence development in important ways throughout life (Thomas *et al,* 1963). However, Partridge and Lerner's (2007) review of the literature challenges this theory. They argue that the developmental course of difficult temperament follows a non-linear trajectory over the first five years of life and note that the different reporting of temperament as either stable, or changing over time, depends on the specific statistical models chosen by researchers (Partridge & Lerner, 2007).

Carey and McDevitt (1978) constructed the Infant Temperament Questionnaire (ITQ) consisting of seventy items extracted from the interview protocol of the nine dimensions of the NYLS, which was later revised and published as the Revised Infant Temperament Questionnaire (RITQ). The RITQ increased the number of items in the ITQ from seventy to ninety-five and rating options from three to six, with more items having high-low reversal (Carey & McDevitt, 1978). This questionnaire was used by Weiss *et al* (2004) who demonstrated that eighty percent of a sample of 152 pre-term, low birth weight infants were classified as having temperaments that were difficult to manage at six months of age. However, many statistical evaluations have been performed, demonstrating that the nine dimensions have conceptual overlap and low internal consistency (e.g., Bohlin *et al*, 1981; Sanson *et al*, 1987). The Early Infant Temperament Questionnaire (EITQ) is a seventy-six item parent questionnaire adapted from the RITQ to be developmentally appropriate for infants of one to four months old (Medoff-Cooper *et al*, 1993).

The Neonatal Behavioral Assessment Scale (NBAS) was developed in 1973 to describe the separate functioning of the interactive, motoric, state, and autonomic systems, as well as their integration, within the healthy, normal, full-term newborn (Brazelton, 1973). The NBAS is composed of twenty-eight behavioural and eighteen reflex items to document the interactive capabilities suitable for infants up to two months old. Hawthorne (2004) suggested that the scale was designed to highlight the positive aspects of the baby’s behaviour rather than examine the baby for pathology as is done with the medical model. By the end of the assessment, the examiner has a behavioural representation of the infant, describing the baby's strengths, adaptive responses and possible vulnerabilities (Costa & Figueiredo, 2011). This scale can only be carried out by a trained and experienced practitioner, which diminishes the risk of parental bias but is unable to capture the range of infant behaviour observed over extended periods and detectable in parent-report questionnaires.

The Alarm Distress Baby Scale (ADBB, Guedeney & Fermanian, 2001) consists of eight items and aims to assess prolonged reactions of social withdrawal in infants. The ADBB was created to help assess social withdrawal in children aged between two and twenty-four months, in the context of routine paediatric physical examination or a psychological assessment, and involves engaging the infant in social behaviour by talking, touching and smiling at him (Costa & Figueiredo, 2011).

The Infant-Toddler Symptom Checklist (ITSC, DeGangi *et al*, 1995) was designed as a parent-report checklist for infants and toddlers from seven to thirty months who experience problems of self-regulation (DeGangi *et al*, 2000). The ITSC includes twenty-four questions with three to five choices about developmental milestones of social communication. These questions focus on the infant's responses in the domains of self-regulation, attention, sleep, feeding, dressing, bathing, touch, movement, listening, language, sound, looking and sight, and attachment/emotional functioning. Wetherby and colleagues (2004) have suggested the ITSC as a highly sensitive and specific tool (both 88.9%) for catching toddlers at risk for developmental delays (including autism spectrum disorders) from a general pediatric sample, though recommend further studies with a larger sample group.

Baby's day diary or Barr chart (Barr *et al,* 1988; Hunziker & Barr, 1986) has been used in studies of infant behaviour and colic (e.g., Fujiwara *et al*, 2011; Hayes *et al*, 2011; Lam *et al*, 2010; Radesky *et al*, 2013; White *et al*, 2000). This diary records parental observations of infant behaviour continuously over twenty-four hours, defined by six hour periods and validated against tape recordings of infants' vocalisations. The Crying Patterns Questionnaire (CPQ) was formulated together with health visitors and general practitioners (St James-Roberts, 1988). As well as recording an infant's sex, birth order and age, it contains seven items, which ask about his/her fuss and crying patterns (although it makes no attempt to distinguish between crying and fussing), and associated parental variables, in the previous week and divides the day up similar to Barr's (1988) 24-hour diary.

The choice of infant behaviour measurement scales for research depends on a number of factors including the study design, the sample size and the age of the participants. The validation and stability of measurement scales, especially for the target age range of the study group, need careful consideration. In addition, Partridge and Lerner (2007) present in their review of the literature, the importance of specific statistical models chosen by researchers when reporting the stability of temperament measurement scales.

7.4 Temperament measurement stability

Although several temperament measurement scales have been developed for researching infant temperament and behaviour, Caspi *et al* (2003) suggest that temperament is not very stable during infancy and only becomes more stable from toddlerhood on. Costa & Figueiredo (2011) analysed differences in infant temperament of ninety-four infants at three and twelve months using the Neonatal Behavioural Assessment Scale (NBAS, Brazelton & Nugent, 1995), and the Alarm Distress Baby Scale (ADBB, Guedeney & Fermanian, 2001) as well as mothers' reports on infant temperament using the Infant Behavior Questionnaire (IBQ, Rothbart, 1981). Stability was observed in most of the temperament's dimensions from three to twelve months old. However there were changes in mothers' perception of infant temperament in terms of level of distress, cuddliness, sadness and approach. The results suggest that infant's characteristics early in life as well as contextual factors influence mothers' perception of infant temperament, with changes across the first year of life (Costa & Figueiredo, 2011).

In contrast to the considerable change in temperament during infancy, temperament appears to be very stable from twenty-four to forty-eight months of age (Lemery *et al*, 1999). Stability of parental report can be due to stability in the child's behavioural style or stability of the parent's perception of the child (Lemery *et al*, 1999). In the Australian Temperament Project, Pedlow *et al* (1993) obtained parent reports of temperament for 450 children from infancy to eight years using revised and shortened versions of the Revised Infant Temperament Questionnaire (Carey & McDevitt, 1978), the Toddler Temperament Scale (Fullard, McDevitt, & Carey, 1984), and the Childhood Temperament Questionnaire (Thomas & Chess, 1977) and concluded that either infant temperament is not as stable as later temperament or that earlier temperament is less adequately measured.

Much of contemporary research concerning the role of temperament in the socio-emotional development of children is based on Rothbart's theory of the structure and development of temperament (Rothbart, 1981; Rothbart & Bates, 2006; Rothbart & Derryberry, 1981). With this approach similar temperament factors are distinguished from infancy on and their views have led to the development and validation of a series of age-specific questionnaires to assess temperament across development (Casalin *et al*, 2011). Questionnaires concerning development of children from birth to five years old include the Infant Behavior Questionnaire (IBQ; Rothbart, 1981) and the Revised Infant Behavior Questionnaire (IBQ-R; Gartstein & Rothbart, 2003) for infants (3-12 months old), the Early Childhood Behavior Questionnaire (ECBQ; Putnam, Gartstein, & Rothbart, 2006) for toddlers (1-3 years old), and the Child Behavior Questionnaire (CBQ; Rothbart, Ahadi, Hersey, & Fisher, 2001) for pre-schoolers (3-5 years old). Putnam *et al* (2008) investigated for fine-grained and factor-level aspects of temperament measured with the Revised Infant Behaviour Questionnaire (IBQ-R), Early Childhood Behaviour Questionnaire (ECBQ), and Children's Behaviour Questionnaire (CBQ). Their research suggested that the ability to gain pleasure from low-intensity activities such as examining books, watching educational television, and playing cognitively demanding board games may allow children opportunities for intellectual growth. In addition, the well-established Revised Infant Behavior Questionnaire (Gartstein & Rothbart, 2003; Rothbart, Chew, *et al.*, 2001) offers possible external validation of developing temperament assessment models to provide new information on parent-observer rating correspondence, in infants as young as one month old, which can extend and elaborate the understanding of infant measurement and behaviour (DeSantis *et al*, 2011).

7.5 Chapter summary

The measurement of infant temperament is an important part of understanding the concept of difficult temperament and unsettled infant behaviour but is challenged by a number of factors. Firstly, many of the temperament measurement methods rely on parental reporting as this is regarded as the most accurate form of information collection over day and night-time analysis. Therefore, parental perception, which may also be influenced by the behaviour of the infant even when the unsettled behaviour has subsided (White *et al*, 2000; Wolke *et al*, 1995), plays a prominent role in temperament recording. Secondly, environmental factors and family circumstances can influence interactions between mother and infant which in turn affects the mother's perception of infant behaviour. Finally, early infancy temperament measurement is limited by a lack of stability in the parent-report documents for very young infants.

Developments in infant temperament measurement have aimed to offer a multi-disciplinary, integrative perspective and a comprehensive analysis of the infant. The value of assessing infant behaviour from an early age is recognised as this may be a predictor of persistent behavioural problems where early interventions would be effective. Choosing the correct parent-report questionnaire for a specific study is paramount so that the most appropriate fit is achieved based on the age group. The temperament assessment tool most established in this field is Rothbarts' Infant Behavior Questionnaire (IBQ), which is discussed in more detail, with its developments and revisions, in the next chapter.

Chapter 8 – Rothbarts Infant Behaviour Questionnaires

Infant temperament has been assessed through the use of structured questionnaires which provide an efficient means for evaluating a wide range of temperament variables. As they are completed by parents, they provide an opportunity to observe infants in a variety of situations and take advantage of care-givers extensive observations. The use of parent-report questionnaires facilitates capturing the behaviours of infants throughout the daytime and night allowing for a more comprehensive representation of reactions to situations. However, the use of parental questionnaires relies on the perceptions of parents, thus such tools are prone to bias (Carey & McDevitt, 1978; Persson-Blennow & McNeil, 1979; Rothbart, 1981).

When examining unsettled infant behaviour, the IBQ is of particular interest as it has been used to demonstrate a link between colic and infant behaviour, particularly in the 'distress to limitations' subscale (White *et al*, 2000). White *et al* (2000) found that infants with 'colic' slept less, cried more and were rated by their mothers as having more difficult temperaments on the IBQ when compared with a matched control group. Stifter and Braungart (1992) had found that measures of colic in early infancy (one to three months) were not predictive of later measures of temperament indicating that less than three months of age was not an ideal time to assess the temperament characteristics expected to demonstrate longitudinal characteristics (Rothbart *et al*, 2001b). However, another group of researchers reported stability between two weeks and twelve weeks and subsequently two months and twelve months for three of the IBQ scales (Worobey & Blajda, 1989).

Much of the recent research into temperament development in children is dominated by Rothbart's theory of the structure and development of temperament

(Rothbart, 1981; Rothbart & Derryberry, 1981). Similar temperament factors identified from infancy led to the development and validation of a series of age-specific questionnaires to assess temperament (Casalin *et al*, 2011). The original IBQ (Rothbart, 1981), was followed by the revised version in 2003 (Gartstein & Rothbart, 2003) and more recently shortened versions of the revised IBQ (Putnam *et al*, 2014). In this chapter, three of Rothbart's questionnaires, the original IBQ, the revised IBQ and the short form of the revised IBQ, are discussed in relation to how they were developed and the impact of these questionnaires on the examination of infant temperament. Challenges associated with validity and stability using these questionnaires, particularly in very young infants, are discussed.

8.1 The original Infant Behavior Questionnaire (IBQ)

The original IBQ (Rothbart, 1981) is a widely used parent-report measurement which consists of ninety-four items using a seven-point numerical scale (never to always) and has been shown to have good reliability and validity (e.g., Bridges *et al*, 1993; Clark *et al*, 1997; Crockenberg & Acredolo, 1983; Fagen *et al*, 1987; Goldsmith & Rothbart, 1991; Reznick *et al*, 1989; Rothbart, 1986, Worobey, 1997). It was developed for infants of three months and older but is also one of the few instruments where reliability, convergent validity, and relative stability have been demonstrated with infants as young as two weeks of age (Worobey, 1986; Worobey & Blajda, 1989). This is important as temperament characteristics are said to be present at birth (Buss & Plomin, 1975; Goldsmith & Gottesman, 1981) and should be expressed in the infant's earliest interactions with its environment (Worobey, 1986). However, measurement of temperament in early infancy using parent-report forms has proven to be difficult due to lack of stability in the measures.

The original IBQ (Rothbart, 1981) attempted to address concerns about potential error associated with parent-report questionnaires (Gartstein & Rothbart, 2003). Parents were asked to report the relative frequency of occurrence of specified infant reactions in concrete situations during the previous one to two weeks, to minimise problems associated with recall and to limit biases associated with more global questions (Gartstein & Rothbart, 2003). Questions concerned the frequency of behaviours with regard to the following categories: Activity Level, Smiling and Laughter, Fear, Distress to Limitations, Duration of Orienting and Soothability (Rothbart, 1981). The Vocal Reactivity scale was not part of the original questionnaire, but was added later as an element of an IBQ validation study (Rothbart, 1986).

Research on infant temperament has evolved substantially since the original IBQ with the development of the Children's Behavior Questionnaire (CBQ; Rothbart *et al*, 1994), followed by the revised IBQ (Gartstein & Rothbart, 2003) from which short and very short forms were then developed (Putnam *et al*, 2014). The CBQ is a 195-item parent-report questionnaire taken from existing temperament questionnaires covering other developmental stages, including the IBQ (Rothbart, 1981). Analyses of the CBQ scales identified three broad factors accounting for the overarching structure of child temperament (Rothbart *et al*, 2001a). The CBQ was developed for assessing temperament in children three to seven years of age and is one of the most widely used measures of child temperament in the field, being cited over 900 times (Kotelnikova *et al*, 2015).

8.2 Revised Infant Behavior Questionnaire (IBQ-R)

The Revised Infant Behaviour Questionnaire (IBQ-R) was created in response to significant advances in research addressing the development of temperament in infants between three and twelve months of age (Gartstein & Rothbart, 2003). Development of the IBQ-R was based on a fine-grained approach to the assessment of infant temperament, allowing examination of detailed constructs of temperament that may be otherwise obscured (Derryberry & Rothbart, 1988). These relations are important as one dimension of temperament may influence the expression of another. The success of the CBQ for children aged three to seven years old suggested that a number of the CBQ scales would provide more detailed and meaningful information regarding individual differences in temperament if tested in the first year of life. Thus, for the IBQ-R, nine new scales taken from the CBQ were examined in the birth to twelve month age range and there were also minor revisions of the six scales of the original IBQ (Gartstein & Rothbart, 2003). The addition of a number of new scales to the IBQ-R facilitated efforts to further study the structure of temperament in infancy via parent-report questionnaires, by allowing researchers to detect a more complex structure (Gartstein & Rothbart, 2003).

The resulting format of the IBQ-R consisted of 191 items scored on a seven-point numerical scale, and measured the following fourteen subsets of temperament: (1) activity level (movement, squirming and locomotor activity), (2) Distress to limitations (fussing, crying or showing distress), (3) Approach (excitement), (4) Fear (distress to sudden changes), (5) Duration of orienting (attention to a single object), (6) Smiling and laughter, (7) Vocal reactivity, (8) Sadness (general low mood), (9) Perceptual sensitivity (detection of slight, low intensity stimuli), (10) High intensity pleasure (related to high stimulus intensity), (11) Low intensity pleasure (related to low stimulus intensity), (12) Cuddliness, (13) Soothability (reduction of fussing and crying in response to soothing techniques) and (14) Falling reactivity (rate of recovery from peak distress and ease to fall asleep).

Rothbart *et al* (2001a) identified three temperament factors in typically developing children: Surgency/Extraversion (positive emotional reactivity), Negative Affectivity (negative emotional reactivity) and Orienting/Regulation (self-regulatory mechanisms of attention /effortful control). These three IBQ broad components can be computed as follows: Surgency/Extraversion - computed from the mean scores of approach, vocal reactivity, high intensity pleasure, smiling and laughter, activity level and perceptual sensitivity; Negative Affectivity - computed from the mean scores of distress to limitation, fear and falling reactivity; and Orienting/Regulation - computed from the mean scores of low intensity pleasure, cuddliness, duration of orienting and soothability.

In developing and expanding the abilities of the temperament domain, which includes a greater number of characteristics, there are increases in the time and effort required of research participants for their assessment. It is estimated that the 191-item IBQ-R takes parents approximately one hour to complete, demanding a significant time commitment. It is impracticable to ask mothers to record prospective information for long periods and the strategy to ask mothers to report recalled crying patterns over the last week or two is recommended (St James-Roberts & Halil, 1991). Therefore, to minimise parental biases associated with poor recall, making abstract evaluations, or comparative judgments, parents are asked in the IBQ-R to report the frequency with which infants have enacted specific behaviours in common situations during the past week or two weeks (Putnam *et al*, 2014).

8.3 Revised Infant Behavior Questionnaire – Short Form

Through the creation and validation of two shorter versions (known as the short form and the very short form), the time requirement for questionnaire completion was reduced. The IBQ-R short form (IBQ-Rs) has ninety-one items and can be filled out in approximately thirty minutes making it a valuable tool for researchers (Putnam *et al,* 2014). The IBQ-Rs was assessed against the reliability of the original IBQ form and it was demonstrated that the abbreviated scales, which approximated the full content of the original scales, were strongly correlated with and exhibited levels of inter-parent agreement that were nearly identical to the IBQ-R. Additionally, it has only slightly lower levels of internal consistency, longitudinal stability, and convergence with observational data compared with the long versions (Putnam *et al*, 2014). However, the comparison of the IBQ-R and IBQ-Rs did not involve administering both to the same sample and a more direct comparison would lead to greater confidence in the correspondence between the IBQ-R and the short form (Putnam *et al*, 2014).

Although there is a rapid pace of infant development between three and twelve months of age, the degree of inter-parent agreement was found to be largely consistent across multiple age points between most scales of the IBQ-R standard and short forms (Putnam *et al*, 2014). However, low inter-parent agreement of Perceptual Sensitivity, in standard and short forms, suggested a degree of subjectivity in parents' ratings. This was considered to be due to the subtlety of behaviours indicating perceptual awareness (Putnam *et al*, 2014). The Soothability and Cuddliness scales also exhibited inter-parent agreement that was substantially lower than that found for other scales (Putnam *et al*, 2014). Gartstein and Rothbart (2003) suggested that low inter-parent agreement for the Soothability scale reflected differences in the effectiveness of different parents soothing methods. Similarly, low inter-parent agreement of the Cuddliness scale might indicate differences between the emerging relationships parents formed with their infant (Parade & Leerkes, 2008).

The IBQ-Rs includes the possible response 'does not apply', which permits parent to indicate they were unable to provide a score as the behaviour and situation in question did not occur in the previous two weeks. The scoring procedure does not differentiate between non-responses and 'does not apply' responses. In a recent prospective, community-based longitudinal cohort study of 401 infants, Giesbrecht *et al* (2014) determined that the rate of 'does not apply' responses in a three month assessment was three times as high (22%) as the rate at six months (7%) using the IBQ-Rs, whereas missing data due to non-response only accounted for <0.2% at both ages. There were noticeable reductions in internal consistency and longitudinal stability associated with missing data, but this problem was limited primarily to assessment of three-month-old infants. The mean number of 'does not apply' items exceeded fifty percent in the Perceptual Sensitivity and Approach scales at three months and two additional scales, Duration of Orienting and High Intensity Pleasure, had 'does not apply' items exceeding thirty percent. None of the scales at six months had mean 'does not apply' rates that exceeded fifty percent and only the Perceptual Sensitivity scale exceeded thirty percent 'does not apply' responses.

The high rate of 'does not apply' responses in the IBQ-Rs challenges the validity of using these scales to assess very young infants. Notably, Gartstein and Rothbart (2003) did not find age-related changes in 'does not apply' responses on the IBQ-R. However, they analysed their data using ranges of age (e.g. 3-6 months, 6-9 months, 9-12 months) rather than analysing at a specified age (e.g. three months, six months, nine months etc.) as in the Giesbrecht *et al* (2014) study and this may have obscured these differences. Worobey and Islas-Lopez (2009) also demonstrated greater utility of the IBQ-R as infants increased in age. They measured temperament at three and six months of age in twenty-four African-American infants using the IBQ-R, and found that although maternal ratings of activity and fussiness did not correlate with more objective measures at three months of age, they were significantly correlated at six months (Worobey & Islas-Lopez, 2009).

Giesbrecht and colleagues (2014) suggest a number of measures to address the issue associated with assessing very young infants to help maintain the quality of data. For example, they suggest delaying assessment until infants are at least six months of age, selecting the full length version of the IBQ-R or using modern missing data statistical techniques. They also recommend excluding the scales in the IBQ-Rs that have high rates of ‘does not apply’ items. Consideration of the use of ’hybrid’ measures depending on the goals and hypotheses of a particular investigation is proposed (e.g. Casalin *et al*, 2012) but should be regarded cautiously when deciding on which IBQ version to use (Putnam *et al*, 2014). Casalin *et al* (2012) demonstrated this by eliminating some of the subscales of the IBQ-R and ECBQ when investigating the replication of higher order factor structure of temperament and longitudinal stability in eight to twenty month old children. The subscale Low-Intensity Pleasure has been shown to play an important role in the stability of the regulatory factor (Putnam *et al*, 2008), and although they (Casalin *et al*, 2012) clearly replicated the three-factor structure, higher stability could have been found if they had not excluded this subscale.

8.4 Chapter summary

The developing study of infant temperament has resulted in numerous measurement tools, which can be selected depending on the suitability to the specific research topic, sample size and age group. Parent-report questionnaires have been found to be particularly important in collecting a lot of data on infant behaviour over long periods. However, parent-report tools are limited by being subject to parental perceptions and bias. More recently, emphasis has been placed on cultivating a questionnaire that limits the subjectivity of the items and enhances objectivity.

Rothbarts IBQ and theory on the structure and development of infant temperament measurement has been significant in guiding the evolution of further measurement structures. Within the three-factor structure (i.e. surgency/extraversion, negative affectivity and orienting/regulation) questionnaires suitable for application in a variety of study types and sizes have been investigated and validated. Most challenging has been validating a temperament measurement tool for very young infants. While early studies supported the use of Rothbarts IBQ in infants as young as two weeks old (Worobey, 1986; Worobey & Blajda, 1989), fifty-seven of the ninety-four items were removed from the analysis (Worobey, 1986) and recent work by Giesbrecht *et al* (2014) also highlights weaknesses associated with the 'does not apply' application within IBQ-R associated with very young infants. Notwithstanding this, Rothbarts IBQ forms are regarded as the most validated, established and widely used questionnaires in current infant behaviour assessment studies.

Chapter 9 – The Osteopathic Perspective

Since the osteopathic profession was founded in the late 19th century it has attempted to define itself in a way that differentiates osteopathy from other therapies. The General Osteopathic Council in the UK define osteopathy as a primary care profession, focusing on the diagnosis, treatment, prevention and rehabilitation of musculoskeletal disorders, and the effects of these conditions on patients' general health (General Osteopathic Council, 2015). Osteopathy can be used to treat people of all ages; a recent national UK pilot collected 1630 standardised datasets and found the age range to be 0-93 years, with 8.6 percent (140) patients aged under twenty and more than half of these being under one-year-old (Fawkes *et al*, 2014). Most reports which claim benefits of osteopathic treatment in children are anecdotal and evidence is poorly researched (Lim, 2006). A key motivation for this study was because of the paucity of research in this field and, of particular interest, is whether osteopathy can play a role in treating infants who present with unsettled behaviour.

However, as noted in chapter 2, researching unsettled infant behaviour, or colic, is problematic, not least because of the inconsistencies in terminology, diagnostics, management and communication between healthcare providers. Recommendations tend towards a multidisciplinary approach to support, information and education (Douglas & Hiscock, 2010). Emphasis is given to addressing parental expectations, understanding developmentally normal crying behaviour and instruction on effectively reading baby cues (Nikolopoulou & St James-Roberts, 2003). The benefits of behavioural intervention programmes and infant handling advice are also documented (Nikolopoulou & St James-Roberts, 2003). A fundamental problem to finding a clear consistent approach to treatment of unsettled infant behaviour is the lack of understanding on causal processes and reliable and valid diagnostic strategies.

Establishing a link between osteopathic treatment of infants and improvement in their unsettled behaviour requires clarification of several assumptions around osteopathy. For example; there is an identifiable physiological process in osteopathic treatment; the musculoskeletal system is influenced by osteopathy; the tests used to examine the musculoskeletal system in infants are reliable; there is a good understanding of the outcome measures of osteopathic treatment; the mechanisms behind treatment approaches are undisputed; birth trauma can cause musculoskeletal injury in infants; and the methods of researching osteopathic outcomes are generally accepted. Without doubt there are several issues surrounding these assumptions. This chapter aims to address these issues by reviewing the available literature. It surveys the practice of osteopathy in the UK and evidence of effectiveness of osteopathic manipulative treatment (OMT) before critically appraising the practice of osteopathy in the cranial field (OCF); a form of osteopathy often used in the treatment of infants and children. Within osteopathy, it is proposed that birth trauma is one of the most common causes of musculoskeletal dysfunction in infants (Frymann, 1966; Sutherland, 1990). This proposal will be critically appraised. This chapter will conclude by examining the difficulties in conducting empirical research in the field of osteopathy, which is needed to enhance practice and to test theory and effectiveness of treatments in order to provide best care for patients.

9.1 Structure and function

Osteopathic manipulative treatment (OMT) is a complementary medical practice that focuses on body health by treating the musculoskeletal framework (Turi *et al*, 2013). A foundational principle of osteopathy is that there is an inter-relationship between the structure and function of the human body i.e. if the structure of the body is not optimal, the function of the body will also be affected (Stone, 1999). Osteopathic treatment is directed primarily at the structure of the body and the aim is to achieve healthy structural balance so that function is not disturbed. Osteopathic practitioners propose that by understanding the relationship between structure and function, the body's self-regulation and self-healing capabilities are enhanced (Cerritelli *et al*, 2013). There are 5,110 osteopaths on the UK Statutory Register of Osteopaths (General Osteopathic Council, 2015). Most osteopaths are trained in paediatric care, and OMT is available for many paediatric conditions (Posadzki *et al*, 2013).

A diagnostic concept, particularly among American trained osteopathic physicians, is that of somatic dysfunction which is defined as:

"Impaired or altered function of related components of the somatic (body framework) system: skeletal, arthrodial, and myofascial structures, and related vascular, lymphatic, and neural elements."

(Educational Council on Osteopathic Principles of the American Association of Colleges of Osteopathic Medicine 2003, p.1249)

The report of prevalence of somatic dysfunction is problematic as it is not clear whether it can be diagnosed in a clinically reliable way (Najm *et al*, 2003; Seffinger *et al*, 2004). According to Cerritelli *et al* (2013), diagnostic criteria for somatic dysfunction focus on tissue texture abnormalities and tone, along with evaluation of areas of asymmetry, misalignment of bony landmarks and quality, balance and organisation of joint motion. Imbalances are believed to cause an increase in energy requirements by affecting the biomechanics of the musculoskeletal system and reducing the efficiency of movement (Carreiro, 2003). Some osteopaths claim that infantile asymmetries in positioning and movement have the potential to affect the infants physical development and cognitive processes through their influence on proprioceptive mapping, motor planning development, respiratory-circulatory function and myofascial relationships (Carreiro, 2008). A retrospective review of data by Pizzolorusso *et al* (2013) found that out of one hundred and fifty-five preterm and term newborns evaluated osteopathically, the highest rate of somatic dysfunction was found in the pelvic area (40.7%) and the occipital bone presented the highest rate of intraosseous lesions. Waddington *et al* (2015) recently described the somatic dysfunction severity score (SDSS) to summarise total somatic dysfunction of the cranial, cervical, lumbar and sacral regions as identified by osteopathic practitioners. They found a relationship between SDSS and length of labour (Waddington *et al*, 2015) but no correlation between somatic dysfunction and duration of second stage labour, maternal parity, mode of delivery or labour augmentation. Previous findings from Sorbe and Dahlgren (1983) found an association between cranial moulding in newborns and length of second stage of labour, primiparity and use of oxytocin augmentation. The reliability of the results from this study should be regarded with caution as measurements of the size and form of the infants' heads were taken from photographic evidence.

Palpatory skills are a central part of OMT (Pizzolorusso *et al*, 2013) with examination and diagnosis from an osteopathic perspective relying primarily on palpation of muscles, joints, fascia and fluids within the human body. Spinal palpatory exams are a primary and well accepted part of the evaluation of spinal pathology in many healthcare professions. However, conflicting data has been reported regarding the reliability of spinal palpatory tests (Najm *et al*, 2003; Seffinger *et al*, 2004). The systematic review of Najm *et al* (2003) assessed the content validity of spinal palpatory tests used to identify spinal neuro-musculoskeletal dysfunction. Overall poor sensitivity was reported for a range of motion studies, with a slightly better sensitivity reported in one study that examined cervical pain. It was concluded that the lack of acceptable reference standards may have contributed to the weak sensitivity findings (Najm *et al*, 2003). Another systematic review evaluating the reliability of spinal palpatory diagnostic procedures found that regional range of motion was more reliable than segmental range of motion, and intra-examiner reliability was better than inter-examiner reliability (Seffinger *et al*, 2004). This study, which used two blinded, independent reviewers to score each article, also found that pain provocation tests were most reliable and soft tissue paraspinal palpatory diagnostic tests were not reliable. In the studies that used kappa statistics, the pain provocation studies demonstrated acceptable reliability (64%), followed by motion studies (58%), landmark (33%), and soft tissue studies (0%). Noteworthy is that examiners' experience level did not improve validity or reliability of palpatory diagnostic tests (Najm *et al*, 2003; Seffinger *et al*, 2004).

Given that manual procedures are a cornerstone towards diagnostic and therapeutic interventions across disciplines, there is a need to enact continuing medical education and research guidelines to address the efficacy of spinal palpatory procedures (Najm *et al*, 2003) and to incorporate more rigor in study design and presentation of results (Seffinger *et al*, 2004). Clinical trials using spinal palpatory diagnostic procedures need to assess the reliability and, if possible, the content validity of the procedures and clinicians need to be cognisant that pain provocation tests are most reliable (Seffinger *et al*, 2004). Infant pain is a specialised topic not only because infants are pre-verbal but also because of clinical difficulty in assessing and measuring pain and acknowledging that infants can have pain without apparent or obvious injury (Finley *et al*, 2005), which makes reliability of research and conclusive statements about osteopathic treatment of babies even more difficult.

9.2 Low back pain and OMT

Not surprisingly, because of the historical preponderance of low back pain as a reason for visiting osteopathic physicians, osteopathic clinical trials have addressed low back pain more often than any other condition (Licciardone *et al*, 2005). In the management of low back pain, there is recognition that whilst explanatory studies have failed to show a convincing benefit for spinal manipulation, more pragmatic studies that have tested packages of care, including manipulation, have shown a benefit (Russell *et al*, 2004; Savigny *et al*, 2009). In a recent double-blinded RCT, Licciardone *et al* (2013) found that patients receiving OMT used prescription drugs for low back pain less frequently during a twelve week study than did patients in the sham OMT group. While this supports the findings of Andersson *et al* (1999), it is in contrast to a previous study by Licciardone *et al* (2005), which reported that patients with low back pain were more likely to use analgesics, nonsteroidal anti-inflammatory agents, or muscle relaxants to complement OMT rather than as an alternative to it. Burton *et al* (2004) recommend that outcomes in back pain trials may best be measured by evaluating changes in the overall impact of the disorder over time, rather than by measures taken at a single time point.

In studying a physical intervention such as OMT, conducting a clinical trial is much more difficult because placebo control and blinding are problematic (Licciardone, 2004). The two types of control groups in OMT trials are those who receive 'sham manipulation' along with their usual care and those who receive usual care without any other intervention. At least two important problems exist with using no-intervention control subjects: the control subjects are likely to deduce their group assignment and they will receive less attention than subjects receiving OMT. Sham manipulation is intended to overcome these problems; however, in the process of providing this intervention, it is possible that some therapeutic benefit may occur, thereby reducing the observed efficacy of OMT (Licciardone, 2004). Psychosocial factors are important in the development of disability and the transition to chronic pain states (Waddell, 1987). According to the biopsychosocial model of illness, all treatments including osteopathy comprise physical, psychological and social components (Burton *et al*, 2004). Biases in the form of increased patient contact between osteopathy patients and therapist provide possible explanations for the psychological benefits of osteopathy, which may also be due to reduction in distressing symptoms or improvement in patients' understanding of spinal pain (Williams *et al*, 2003).

9.3 The musculoskeletal system and OMT

A relationship between dysfunction in the musculoskeletal system and unsettled infant behaviour has been implicated by specialist neurologists, physiotherapists and orthopaedic surgeons (Biedermann, 2006; Gudmundson, 2010; Holsti and Grunau, 2007; Papousek & Hofacker, 1998). A functional problem in the cervical spine has been proposed as a cause of crying; the therapeutic effect being mediated through a somatovisceral or spino-craniovisceral reflex (Biedermann, 2005; Hipperson, 2004). Compression at the base of the skull from the birthing process has also been suggested (Kotzampaltiris *et al*, 2009; Soltis, 2004). In a narrative literature review, Lim (2006) suggests an improvement of unsettled infant behaviour following OMT; however, the evidence to support these claims remain weak. A recent addition to the osteopathic principles (Rogers *et al*, 2002) is a statement giving ascendancy to the role of the musculoskeletal system in health and disease, which also acknowledges the important metabolic processes occurring within the musculoskeletal system. An inter-relationship between adverse conditions in the musculoskeletal system and consequences in the nervous, endocrine, immune, cardiovascular, respiratory and digestive systems is also suggested (Evans, 2013).

A relationship between OMT and reduction in length of stay in hospital (LOS) for pre-term infants has been reported in several studies (Cerritelli *et al*, 2013; Cozzolino *et al*, 2010). A randomised controlled trial (RCT) by Cozzolino *et al* (2010) on a sample of 101 premature infants without any medical complications showed that the application of OMT in the neonatal intensive care unit (NICU) significantly reduced LOS. These findings were supported by two further studies; an RCT on 110 preterm newborns admitted to a single NICU between 2008 and 2009 (Cerritelli *et al*, 2013) and an observational prospective study of 352 preterm infants (Pizzolorusso *et al*, 2011). Pizzolorusso *et al* (2011) also suggested that OMT may reduce the occurrence of frequent symptoms of abnormal gastrointestinal functionality. Moreover, the absence of adverse events and side effects was widely reported, thus providing evidence that the approach is safe

(Cerritelli *et al* 2013, 2014). The results of these studies should be regarded with caution as testing was conducted in one single NICU and by the same research department. Therefore, a multi-centre allocation is needed to generalize these results to a broad population of high risk newborns.

Further small studies have been conducted to evaluate the effects of OMT in paediatric care. In a RCT, Vandenplas *et al* (2008) found polysomnography evidence that OMT reduced the incidence of obstructive apnoea's during sleep in twenty-eight healthy infants (six to eighteen weeks old) with a previous history of obstructive apnoea. Mills *et al* (2003) reported a potential benefit of OMT for treating children with recurrent acute otitis media. Another RCT by Nemett *et al* (2008) investigated the effectiveness of osteopathy in treating paediatric dysfunctional voiding in twenty-one children (four to eleven years old) and found a significantly greater improvement in short-term outcomes in children compared to those in standard care. These results support Alcantara and Mayer's (2008) findings on the benefits of spinal manipulation for treating children with constipation. There is a suggested role for OMT in modulating and reducing the inflammatory status of infants through the anti-inflammatory mechanism; although this hypothesis needs further examination (Degenhardt *et al*, 2007; Meltzer & Standley, 2007). There is also some weak evidence of an association between autonomic nervous system function and myofascial release technique, which is an element of OMT (Henley *et al*, 2008). These results should be taken with caution as treatment allocation was neither randomised nor structured, and procedures were not blinded.

Although studies evaluating the effectiveness of OMT have been conducted, many have methodological limitations such as small sample groups, no control group and other factors that increase the risk of bias. Those studies that yield positive findings for OMT are not supported by subsequent research with more robust methodologies. Osteopathy in the cranial field, which is an osteopathic practice often employed in the treatment of infants and children, is even more vulnerable to criticism.

9.4 Osteopathy in the cranial field – critically appraised

Osteopathy in the cranial field (OCF), also referred to as craniosacral therapy, cranial osteopathy or cranial osteopathic manipulative medicine, is an approach to treatment that uses passive palpation of micro-movements in all parts and tissues of the body, including the head (Wilkinson *et al*, 2015). In the UK, the National Council for Osteopathic Research (NCOR) found that twenty-six percent of osteopathy patients had received treatment involving cranial techniques (Fawkes *et al*, 2010). This survey also found that osteopaths working in the cranial field, when compared with general osteopaths, appear to treat a smaller proportion of patients presenting with problems in the lumbar spine area (19% v 36%) and a higher proportion of patients presenting with head/facial problems (17% v 7%). A survey by KPMG on behalf of the GOsC looking into how osteopaths practice, found that only seven percent of osteopaths practice OCF more than ninety percent of the time but that seventy-six percent of osteopaths carry out some form of OCF (KPMG, 2011). A survey of members of the Australian Osteopathic Association found that thirteen percent used cranial techniques eighty to one hundred percent of the time (Orrock, 2009).

Sutherland (1899) developed OCF, which focused on the articulations between the bones of the skull (as cited in Sutherland, 1990). Practitioners of OCF believe that rhythmic motion of the cranial bones exists due to fluctuations of the cerebrospinal fluid pressure (Rogers & Witt, 1997) and arterial blood pressure (Ferguson, 2003) and called this the primary respiratory mechanism (PRM). The fundamental theory behind the cranial techniques used during OCF is that passive palpation can be used to detect spontaneous or rhythmic movement of cranial bones, and the application of selective pressure to the cranial bones can manipulate the rhythmic movement of the bones and intracranial fluids to achieve a therapeutic outcome (Magoun, 1966; Rogers & Witt, 1997; Sutherland, 1990). However, since its beginnings OCF has been the subject of controversy. While proponents of OCF claim that gentle manipulation re-establishes motion and subsequently improves blood flow and drainage, ultimately allowing healing to occur in a cranial strain (Frymann, 1966;

Magoun, 1951; Sutherland, 1990), the lack of evidence supporting Sutherland's model of the underlying physiology has led to the proposition of a number of alternative hypotheses such as; arteriolar vasomotion, reversible venous flow, the circulation of CSF, the sympathetic nervous system (Ferguson, 2003), an energetic-based model (McPartland & Skinner, 2005) and tissue mechanics (Cowin & Doty, 2007; Gabutti & Draper-Rodi, 2014).

The nature of the minute adjustments and corrections in OCF is difficult to demonstrate and consequently, researching this mechanism can be challenging. In a literature review, Seimetz *et al* (2012) illustrated that both externally applied forces and increases in intracranial pressure result in measurable motion across the cranial sutures in adolescent and adult mammalian species, and measurable changes in cranial vault diameter in post-mortem and living adult human skulls. They reported that given the forces required to be used during OCF, it is reasonable that small amounts of cranial deflection can occur as a result of the forces applied to the skull during OCF. However, previous research demonstrated no significant changes in coronal suture movement when low loads of force, similar to those used clinically in OCF, were applied to rabbits and therefore suggesting the need to explore a different biological basis for OCF (Downey *et al*, 2006). In addition, the exact standardisation of cranial manipulative procedures is difficult as demonstrated in a cross-sectional study by Zegarra-Parodi *et al* (2011), who found the application of cranial palpation to be extremely variable in forty-three registered osteopaths using a Flexiforce tactile force sensor device. Others have found that PRM rates cannot be palpated reliably and under certain conditions were influenced by the examiners' respiratory rates (Sommerfeld *et al*, 2004). Equally problematic is that there are limitations of available technology that can make reproducible and reliable measurements so that the phenomena involved in OCF can be better understood (Ferguson, 2003).

In spite of claims made about the effectiveness of OCF, to date research on treatment effectiveness constitutes low-grade evidence conducted using inadequate research protocols with a high risk of bias (Ernst, 2012; Green *et al*, 1999). There has been little research into OCF and that which is available is not definitive or consistent. There is no existing evidence as to whether cranial motion contributes to the reduction in symptoms that result from OCF (Seimetz *et al*, 2012). The clinical practice of OCF seems to have some anecdotal success; however many claims are based on personal experiences in osteopathy and writings handed down by over a century of osteopaths. For many practitioners the extent of anecdotal confirmation supporting both the descriptive model and clinical outcomes is interpreted as sufficiently compelling to justify continued use of cranial treatments in clinical practice. The majority of research specifically looking at OCF has focussed on the outcomes of care in several disorders including tension headache (Hanten *et al*, 1999), cerebral palsy (Duncan *et al*, 2008; Wyatt *et al*, 2011), infantile colic (Hayden & Mullinger, 2006), infantile gastroesophageal reflux (Joyce & Clark, 1996), breastfeeding problems (Wescott, 2004) and visual function (Sandhouse *et al*, 2010). Kotzampaltiris *et al* (2009) suggest that an abnormal PRM at two weeks of age may be associated with excessive crying. However these are generally small-scale studies with small sample sizes and of variable quality. A number of systematic reviews have found that the currently available evidence on the clinical efficacy of cranial osteopathic manipulative medicine is heterogeneous and insufficient to draw definitive conclusions and an improvement in methodological quality in future studies is needed (Ernst, 2012; Green *et al*, 1999; Jäkel & von Hauenschild, 2011).

More recently Wilkinson *et al* (2015) conducted a prospective cohort study of practitioners and their patients to describe the practice of UK osteopaths using OCF. One in five eligible practitioners (58/270) participated in the study and completed an enhanced standardised questionnaire for ten consecutive patients attending for a new episode of care and a patient reported symptom severity item was included. Many patients reported a significant reduction in symptom severity scores following an average of three treatments and any adverse treatment reactions appeared to be transitory in nature. However, this study lacked a control group and, therefore, direct causality to these findings cannot be attributed with certainty to OCF treatment. Patient improvement may be attributed to several different mechanisms such as relaxation of muscles due to massaging effects, or a decrease in pressure on the cranial nerves due to massaging (Seimetz *et al*, 2012). Placebo effect may also play a role although Cerritelli *et al* (2012) queries the effect of placebo in newborns when sham treatment was shown to have no effect in their double-blinded randomised control trial on 250 preterm newborns. The non-specific effects of reassurance, attention and support provided to parents during the osteopathic consultation (Lim, 2006), as well as the natural regression to the mean (Senn, 2011), cannot be ruled out.

In spite of the positive effects attributed to OCF treatment by many (Brough *et al*, 2014) current scientific evidence does not support the commonly accepted theoretical models of OCF. Evidence of the effectiveness of cranial manipulative treatment is yet to be established (Green *et al*, 1999) and reliable research has not been able to validate the concepts and practice (Ferguson, 2003). In a qualitative study, Brough *et al* (2014) identify the quality of the therapeutic relationship between patient and practitioner as a necessary component of successful treatment and suggest the development of a new outcome measure that encompasses mind, body and spirit. Moran and Gibbons (2001) reported no intra-or inter-examiner reliability of the diagnostic ability of experienced therapists and Ernst (2012) concludes that there is insufficient evidence to suggest that OCF has therapeutic effects beyond placebo. Therefore, further research is required to investigate the effects of cranial motion in OCF on patient improvement.

9.5 Birth Trauma

Birth injury, unless major and life threatening, is under-recognised and under-treated (Gottlieb, 1993). Pressler & Hepworth (2000) suggest two levels of birth trauma: major birth trauma and transient mechanical birth trauma (TMBT). Major birth trauma, which includes central nervous system injuries, muscle damage, bone fractures and lacerations, is known to be a risk factor of infant mortality and morbidity. TMBT includes moulding, cephalohematoma, subconjunctival haemorrhage, body bruising, facial bruising, petechiae, forceps marks and diminished arm movements. O' Doherty (1985) demonstrated the moulding effects on the newborns' cranium following awkward delivery presentations in birth and Nelson (2007) associated overriding parietal bones, sometimes observed in cranial moulding, with caput succedaneum. However, widely differing opinions arise concerning the lasting effects of these forces (Allen, 2005). It seems to be generally thought that the effects of the forces spontaneously resolve once the forces are removed and many medical practitioners propose that TMBT has no lasting impact (e.g. Fabamwo *et al*, 2006). Although osteopaths diagnose and treat birth trauma (Magoun, 1951; Arbuckle, 1971) the techniques used involve specific osteopathic palpation, which are difficult to measure and their efficacy is not, to date, supported by research.

Some osteopaths consider the process of birth to be one of the most common causes of strain in an infant's musculoskeletal system (Frymann, 1966; Sutherland, 1990). These strains are proposed to occur in circumstances where the infants head is subjected to excessive compression due to long or difficult labour, ventouse or forceps use, or the delivery is a caesarean section (Frymann, 1966; Lloyd, 2002, Treganza, 1973). Those at increased risk of musculoskeletal injury are the male children born of primapara mothers with assistance methods (Levine *et al*, 1984; Stellwagon *et al*, 2008; Torvaldson *et al*, 2006). In a study of 1250 newborns, Frymann (1966) suggested (by using osteopathic palpation techniques) that severe trauma was inflicted on the heads of ten percent of babies either before or during labour. Frymann proposed that the trauma was associated with strains in the articular membranes of the cranial base (Frymann, 1966). However, it is important to note that these findings have not been reproduced using standard medical examinations.

Osteopathic treatment is based on the theory that any stresses, before, during or following the birth can cause moulding of the infants' head, which creates strain between the cranial bones. The vault of the newborn skull is a membranous structure with the bone plates designed to overlap to aid in the passage through the birth canal during birth. The bones of the base develop from cartilage. Some osteopaths believe the occiput is most vulnerable to strain in the process of birth.

The hypoglossal nerve passes through the cartilage between the basilar and condylar parts of the occiput. The hypoglossal is the motor nerve to the tongue and its physiological function is of primary importance to the sucking and swallowing mechanism. Immediately anterolateral to the articulation between the basilar and condylar parts is the jugular foramen, through which the vagus, glossopharyngeal and accessory nerves pass. The glossopharyngeal nerve is concerned with swallowing and the vagus nerve has many functions associated with the digestive, respiratory and cardiac systems. Distortion to the parts of the occiput may disrupt the functions of these nerves. For example, vagal disturbance has been connected with respiratory, cardiac and digestive disturbance, including vomiting in the newborn (Frymann, 1966; Frymann, 1998). It has also been hypothesised that unsettled infant behaviour is possibly the result of vagal nerve irritation associated with strain patterns in the infants cranium caused during the process of birth (Magoun, 1951).

A recent study found instrumental delivery to be responsible for most cases of neonatal birth trauma (Linder *et al*, 2013). Forceps deliveries were associated with skull fractures, cranial nerve palsies, brachial plexus injuries, facial nerve injuries and torticollis (Sauber-Schatz *et al*, 2010). Cephalohematomas and cranial fractures have been associated with ventouse delivery (O'Mahoney *et al*, 2010). Even under normal conditions, significant traction and rotation of the baby's head during delivery can produce sufficient force to cause clavicle fracture in up to ten percent of vaginal births (Mavrogenis *et al*, 2011; Miller *et al*, 2013). In addition, forty-six rib fractures, undetected at birth, have been reported in the literature (Van Rijn *et al*, 2009). In a peer-reviewed biomedical literature search related to birth injury and musculoskeletal assessment of the injuries, the evidence suggested that infants may receive musculoskeletal injuries through both traumatic and non-traumatic births (Miller *et al*, 2013). This review found up to seventy-three percent of infants had one or more asymmetries stemming from birth (sixty-one percent of those were head asymmetries, forty-two percent were facial and sixteen percent were torticollis). There are varying reports on the incidence rate of torticollis at 1.2 percent (Cheng & Au, 1994), 3.92 percent (Chen *et al*, 2005) and 16 percent

(Stellwagen *et al*, 2008) and incomplete musculoskeletal examination is a possible reason for discrepancies in reporting.

According to Guyer and colleagues (2009, 2012) birth difficulty is negatively associated with the likelihood of breastfeeding. Carreiro (2003) proposes that asymmetry in the position of the clavicles or scapula due to birth related trauma can interfere with the efficiency of breastfeeding due to altered tone of the muscle attachments of the hyoid bone, which is directly related to tongue movement required in infant suckling. According to Frymann (1966), when membranous articular strains in the cranium are resolved through osteopathic treatment, common problems of the neonatal period including feeding and sucking difficulties, vomiting, nervous tension and irregular respiration are overcome. Vacuum extraction has been shown to be a strong predictor of early cessation of breastfeeding due to injury (Hall *et al*, 2002). Such adverse effects have also been associated with epidural analgesia (Tamagawa & Weaver, 2012). In a narrative review Wescott (2004) suggests a gaining recognition of cranial osteopathy for the treatment of breastfeeding problems resulting from birth trauma (Wescott, 2004). A review of 114 case studies showed that seventy-nine percent of new mothers presenting for infant breastfeeding problems were able to exclusively breastfeed after a short episode of manual therapy (Miller *et al*, 2009). However, this research was limited by reliance on group decision making studies and expert opinion rather than randomised controlled trials.

To date, the use of OMT during labour has been limited (Hart, 1918; Whiting, 1911) although its effects are proposed during pregnancy (King *et al*, 2003; Licciardone *et al*, 2010; Turi *et al*, 2013). A randomised, placebo-controlled trial was conducted to compare usual obstetric care and OMT, usual obstetric care and sham ultrasound treatment, and usual obstetric care only. In this study Licciardone *et al* (2010) demonstrated that OMT slowed or halted the deterioration of back-specific functioning during the third trimester of pregnancy. In an exploratory study of 119 women, Turi *et al* (2013) found a positive effect on vaginal tears, Apgar scores and umbilical pH levels when OMT was administered during delivery, in addition to ordinary care. Although the role of osteopathic care in the treatment of pregnant mothers, the newborn and infants has been considered, evidence remains weak (Sullivan, 1997) and a clear relationship between birth trauma and unsettled behaviour has not been established (Lim, 2006). The use of a musculoskeletal screen to identify discomfort in the musculoskeletal system, possibly associated with birth trauma, needs further examination (Miller *et al*, 2013).

9.6 Researching the osteopathic theory

The effectiveness of OMT for paediatric conditions remains unknown, but the existing evidence suggests that the interventions tested have modest effects if at all (Ernst, 2012; Green *et al*, 1999). One major issue is that the RCT is designed for a biomedical model of healthcare and it sits toward the top of the evidence hierarchy (Sackett, 2000). To be clinically useful the results must also be relevant to a definable group of patients in a particular clinical setting; this is generally termed external validity, applicability, or generalisability (Rothwell, 2005). The RCT assumes homogeneity of patients, and fails to recognise the individuality of the patient and their illness experience, which is one the central pillars of the patient-centred care model (Mead & Bower, 2000). In addition, clinicians focus is mainly on the physical effects of the disease, whereas patients are more concerned about different factors such as mental health, emotional wellbeing, general health, and vitality, which are often not measured in RCTs (Rothwell, 2005). How these factors are taken into account in the design and performance of a RCT and in the reporting of the results can have a major effect on external validity (Rothwell, 2005). Posadzki and colleagues (2013) demonstrated this in their critical evaluation on the effectiveness of OMT as a treatment of paediatric conditions, finding only five of the seventeen RCTs included in their review were of high methodological quality and only one of those favored OMT (Posadzki *et al*, 2013). Whether this suggests that the use of RCT is inadequate in fully researching the benefits of OMT, or that OMT is not an effective approach to treatment, requires more examination.

Whole systems research emphasizes the importance of congruence between research methodology and the paradigm of the system being investigated (Verhoef *et al*, 2005). The RCT design is not necessarily incompatible with whole systems research. RCTs could improve generalizability by basing protocols on usual practice (Hawk *et al*, 2007). Case reports could contribute more to whole systems research by increasing their emphasis on patient characteristics and patient-based outcomes (Hawk *et al*, 2007).

Other manual therapies have similar difficulties in producing research of high methodological quality. The review of Dobson *et al* (2012) on manual therapies for colic found that the studies included in this meta-analysis were generally small and methodologically prone to bias, making it impossible to arrive at a definitive conclusion about the effectiveness of manipulative therapies for infantile colic. The benefits of chiropractic therapy for treating infantile colic has been reported (Klougart *et al*, 1989) but research lacks scientific rigor (Alcantara & Anderson, 2008) and has been disputed (Mirtz *et al*, 2009; Olafsdottir *et al*, 2001). In a RCT by Landgren (2010) the benefits of minimal acupuncture for infants with colic was demonstrated but this was later contradicted by Skjeie *et al* (2013). A review on massage therapy showed that the application of a ten to fifteen minute massage led to an improvement of weight gain and to a LOS reduction (Field *et al*, 2010). However, a Cochrane review suggested that these findings were inconsistent and highlighted many methodological concerns of low quality, risk of bias and non-blinding (Vickers *et al*, 2004).

The use of single system research designs (SSRD) in osteopathic research needs consideration. This method appears to present the possibility for clinicians to document their work in a scientific manner and has the added advantage of assessing and tracking individual responses to interventions (Sanders, 2003). SSRDs use statistical techniques and quantitative research methods in a prospective manner to examine the effectiveness of an intervention, and can be used to measure whether the treatment suggested by a RCT is effective on individual patients (Sanders, 2003). However, caution is required with such research methods as small trials tend to inflate results and there is an increased risk of bias in favour of the intervention. Therefore, the RCT cannot be disregarded, particularly with the view of taking a pragmatic approach to examine if its utility is more suitable for osteopathic research.

9.7 Chapter summary

Evidence for the effectiveness of osteopathic treatment is weakened by a paucity of research and lack of rigor within the research that does exist. Those studies that yield benefits for OMT have not been supported by subsequent testing. Research into the practice of OCF is even more problematic given the limitations in performing reliable measurements of techniques (Ferguson, 2003) and the lack of existing evidence for the contribution of cranial motion in patient symptom patterns (Seimetz *et al*, 2012). In a recent systematic review, Jäkel & von Hauenschild (2011) concluded that the currently available evidence on the clinical efficacy of OCF remains insufficient to draw definitive conclusions.

Unless the mechanisms involved in osteopathic treatment techniques, including OMT and OCF, can be elucidated then patient improvement may be attributed to several different mechanisms such as relaxation and placebo (Seimetz *et al*, 2012). Equally, in the treatment of infants with unsettled behaviour, the non-specific effects of reassurance, attention, and support provided to parents during the osteopathic consultation cannot be ruled out (Lim, 2006). This possibility is supported by earlier findings in the literature that highlight infant behaviour programmes and parental support and education as beneficial approaches to managing unsettled infant behaviour. However, unsettled infant behaviour remains a significant problem and what is not yet clear is if there is an element to this condition that involves disturbances in the musculoskeletal system of the infant, possibly associated with birth trauma, and which can be treated using osteopathy. The impact of attention to infant handling, which has been identified in managing these infants, may be a valuable indicator for this theory.

Chapter 10 – Asymmetry in Infancy

Asymmetry in infancy is a clinical condition with a large spectrum of features, expressing an abnormal shape of parts of the body or unequal postures and movements (Van Vlimmeren, 2004). It has a wide variation in appearances (shape, posture, and movement), aetiology, localisation, and severity (Nuysink *et al*, 2008) and can be either persistent or resolving. Both endogenous and exogenous factors are thought to play a role in infantile asymmetries. Genetic disposition, as shown by a family history of scoliosis, rapid growth, reduced muscle tone, and reduced motor activity are presumed to be endogenous factors (Wynne-Davies, 1975; Mc Master, 1983). Exogenous factors include intrauterine and postnatal constraint, and birth injuries (Cheng & Au, 1994, Deidrich *et al*, 2002; Lloyd-Roberts & Pilcher, 1965; Rosegger & Steinwendner, 1992; Wynne-Davies, 1975). Asymmetry is frequently found in newborns (Ronnqvist, 1995) and its clinical significance has to be carefully examined (Biedermann, 2005).

As asymmetries rarely present as a single deformity, terms used to describe these conditions vary depending on the pronounced features, e.g. plagiocephaly (also known as flat head syndrome, positional head deformity or cranial moulding), torticollis (asymmetrical head or neck position), scoliosis (abnormal curvature of the spine), hip dysplasia and foot malposition (or talapase) (Binder *et al*, 1987; Brunetaeu & Mulliken, 1992; Canale *et al*, 1982; Cheng & Au, 1994; Mc Master, 1983; Walsh & Morrissy, 1998). These musculoskeletal abnormalities are observed in babies who are otherwise healthy (Philippi *et al*, 2004) and most may be evident from birth. Scoliosis is rarely apparent at birth (Ventura *et al*, 1998) and is suggestive of a postnatal pressure hypothesis rather than ante-natal for this condition (Winter, 1976; Mau, 1981; Gladel, 1978). Keesen *et al* (1993) stress the importance of asymmetries in perception and posture for the development of more severe consequences.

An association between musculoskeletal abnormalities or infantile asymmetry and unsettled infant behaviour has not been demonstrated. This may be because much is still not understood about unsettled infant behaviour, except that the processes involved are complex and research terminology and design are inconsistent. Thus conclusive evidence is difficult to determine. Previous chapters have explored the topics associated with unsettled infant behaviour and infant temperament. In this chapter, infantile asymmetry is explored in detail, with reference to some of the more common aetiological musculoskeletal conditions. The history of the presentation of asymmetry in infants is briefly documented. This is followed by examining the conditions most associated with asymmetry in infancy including positional preference, deformational plagiocephaly, craniosynostosis and congenital muscular torticollis. Emphasis is given to deformational plagiocephaly, an asymmetrical cranial presentation of increasing significance since the 'back-to-sleep' recommendations for prevention of sudden infant death syndrome (SIDS). The problem of measuring asymmetry in a clinical setting, using a non-invasive method, is presented. This chapter concludes with examining the relatively new term of 'infantile postural asymmetry' and an associated measurement scale, both described and developed by Philippi *et al* (2004; 2006a) to encompass all of the idiopathic asymmetries.

10.1 Persistent and resolving asymmetry

Early studies on postural asymmetries in infancy have described them in relation to asymmetrical head-turning such as asymmetrical skull (Rischbeith 1963, Paine & Oppe, 1966; Epstein & Epstein, 1967), infantile postural scoliosis (Scott, 1956; Lloyd-Roberts & Pilcher, 1965; Shionoya, 1969; Wynne-Davis, 1975), torticollis and a variety of minor structural asymmetries (Rischbeith, 1963). James (1951) described resolving infantile scoliosis of unknown aetiology and, therefore, called it ‘idiopathic’. There can be some overlap between these conditions and when the entire symptom complex is considered this can be referred to as a positional preference (Philippi *et al*, 2006b).

The initial presentation of a positional preference might be a symptom of a more serious persistent infantile asymmetry of spontaneous movements, muscle tone, automatic responses, and reflexes and may be a clue to hemiplegia, cervical plexus injury, disturbances of spine segmentation, or other neuromuscular disorders (Brett, 1991, Cioni *et al*, 2000; Philippi *et al*, 2006b). The development of normal movements in infants represent the most complex spontaneous movement patterns during the newborn period (Cioni *et al*, 2000). These are the gross movements involving the whole body, observable from foetal age (de Vries *et al*, 1982) until about five months of post-term age (Prechtl *et al*, 1997) and can be used in the assessment of early neurological signs of abnormality and asymmetry. Persistent infantile asymmetry requires diagnosis of the underlying aetiology and appropriate management.

10.2 Positional preference

The prevalence of an asymmetric positional preference has been reported as twelve percent of all newborns (Nuysink *et al*, 2008) and it is normally termed ‘idiopathic’ as the cause is unknown in most patients (Canale 1982, James 1975). The main diagnostic feature of a positional preference is the asymmetric limitation of mobility, which is more easily detected after exogenous stimulation (Philippi *et al*, 2004). It should be possible to rotate the head of a newborn ninety degrees in both directions (Chang *et al*, 2001). There is some concern that asymmetries of posturing in infancy may influence functional development (Konishi *et al*, 2002; Miller & Clarren, 2000) and predict the development of scoliosis (Mc Master, 1983; Brunetaeu & Mulliken, 1992; Cheng & Au, 1994).

A right sided preference for cervical rotation and preferential head orientation in most normal newborns while supine has been widely reported (Geerdink *et al*, 1994; Hopkins *et al*, 1987; Turkewitz & Creighton, 1974). Michel (1981) suggested that hand preference might be directly influenced by head orientation, since an infant whose head was turned to one side could see only the arm on that side, giving that arm an advantage in visually guided reaching (Robson, 1968, Coryell & Michel, 1978, Michel & Goodwin, 1979). However, different theories have been proposed for left handedness that do not support this claim including a male predominance (Pekkarinen *et al*, 2003), genetic predisposition (Mc Manus *et al*, 2013), perinatal complications (Liederman & Coryell, 1982) and increased use of ultrasonography during pregnancy (Salvesen & Eik-Nes, 1999).

The infant's head is malleable and growing rapidly, hence it is susceptible to deformation, especially when infants develop a positional preference of the head when lying in the supine position (Boere-Boonekamp & van der Linden-Kuiper, 2001). Positional preference is the most significant cause of deformational plagiocephaly (explained in the next section) especially if it is present at birth and already causing flattening of the occipital bone on one side (van Vlimmeren *et al*, 2008).

10.3 Deformational Plagiocephaly

Plagiocephaly is a skull asymmetry and two mechanisms can be distinguished: malformational plagiocephaly secondary to premature synostosis (or fusing) of a cranial suture (also called synostotic plagiocephaly or craniosynostosis) and deformational plagiocephaly without synostosis, which involves an architectural cranial base asymmetry without growth defect (Captier *et al*, 2003). Deformational plagiocephaly (DP) describes a multiplanar, three-dimensional deformity rarely isolated to a single location on the cranium, characterised by an asymmetrical occipital flattening with a resulting ipsilateral forehead bossing (Pogliani *et al*, 2014). An ipsilateral ear shift in a more anterior position is frequently found; ear height, however, is symmetric and the cranial sutures are not affected (Robinson & Proctor, 2009). A ‘parallelogram-shaped’ head is suggestive of DP (Biggs, 2003). The newborn’s cranium is extremely soft and malleable in order to assist with passage through the birth canal. DP is caused by consistent pressure being placed on a particular part of an infant’s head (Biggs, 2003; Najarian, 1999) that can occur either ante- or post-natally (Pogliani *et al*, 2014).

- 10.3.1 Prevalence of DP

The prevalence of DP was recently estimated at twenty percent as measured by the oblique cranial length ratio (Pogliani *et al*, 2014) which was significantly higher than two earlier studies finding the prevalence of thirteen percent (Peitsch *et al*, 2002; Wynne-Davies, 1975) and may be due to less restrictive inclusion criteria in the recent study (Pogliani *et al*, 2014). DP has become more prevalent since the ‘back to sleep’ campaign for infant sleeping position to protect against sudden infant death syndrome (SIDS) (Kane *et al*, 1996, Philippi *et al*, 2004; Sergueef *et al*, 2006; Van Vlimmeren, 2004). Although several studies have identified the ‘back to sleep’ position as the main cause of DP, additional maternal, pregnancy, delivery and foetal predisposing conditions are thought to play a role (McKinney *et al*, 2008; Peitsch *et al*, 2002; van Vlimmeren *et al*, 2007). Shamji *et al* (2012) showed males to be disproportionately affected over females, and a preponderance of right-sided disease. This supports earlier studies (Boere-Boonekamp, & van der Linden-Kuiper, 2001) and shows similarities with positional preference (Geerdink *et al*, 1994; Hopkins *et al*, 1987; Turkewitz & Creighton, 1974).

- 10.3.2 Risk factors for DP

Several risk factors have been associated with DP which include premature birth, hypotonic muscle disorders, congenital torticollis, intrauterine constraint (such as in multiple gestation or oligohydramnios), pregnancy complications, assisted vaginal delivery, foetal positioning in utero, prolonged labour; abnormal birth position, supine sleeping, preferential head position/positional preference and male gender (Argenta *et al*, 1996; Bridges *et al*, 2002; Cunningham & Heike, 2007; Dunn, 1976; Golden *et al*, 1999; Joganic *et al*, 2009; Kane *et al*, 1996; Kelly *et al*, 1999; Littlefield *et al*, 1998; Littlefeld *et al*, 1999; Littlefield *et al*, 2002; Pietsch *et al*, 2002; Pogliani *et al*, 2014; Turk *et al*, 1996). Joganic *et al* (2009) explain the relationship between prematurity and DP to be a result of decreased activity levels and motor coordination. The association with multiparity is likely because of the constraints in utero and pressure from the maternal pelvis (Joganic *et al*, 2009).

An early study of infants twenty-four to seventy-two hours after delivery showed that thirteen percent had lateral or posterior flattening of the head (Wynne-Davies, 1975) supporting the intrauterine constraint theory. Others in support of the pressure-moulding theory have observed that in DP, the convex side of a scoliotic curve and hip dysplasia all occur on the same side (Dobbs & Weinstein, 1999; Lloyd-Roberts & Pilcher, 1965; Wynne-Davies, 1975) while Konishi *et al* (1986) suggest an association between skull asymmetry and asymmetrical trunk posture, with the convex side of the spine being opposite to the flattened occiput. Observations by Philippi *et al* (2006b) suggest that the most severe examples of asymmetric cervical lateral flexion (picked up by qualitative documentation) are correlated with the intrauterine position. It has also been suggested that mechanical compression forces acting on the mother’s uterus could affect the growing foetus. For example, some authors claim that dysfunction in the mothers’ sacroiliac joints can affect the pelvic diameter and cause constraint to the infants head resulting in an asymmetrical posture (Sergueef, 2007) though there is no supporting evidence for this theory.

In contrast, research from Vles *et al* (1991), did not find persistent individual head orientation preference in healthy, full-term infants within twenty-four hours after delivery, or a relationship between the intrauterine birth position and the head orientation preference. Similarly Boere-Boonekamp & van der Linden-Kuiper

(2001) reported no relationship with multiple/single pregnancies, volume of amniotic fluid, delivery mechanism, use of ventouse or forceps, complications of vaginal delivery or sleep position in the first week of life.

- 10.3.3 Significance of sleep position

Sudden infant death syndrome (SIDS) is defined as death that occurs in infants less than one-year-old, is unexpected, and cannot be explained by information collected during an investigative post-mortem examination (Chizawsky & Findlay, 2005). The implementation of supine sleeping has successfully reduced the incidence of SIDS worldwide. Since the initial recommendation by the American Academy of Pediatrics in 1992, there has been a forty-four percent decline in the SIDS rate from 1.20 per 1,000 live births to 0.67 in the United States (Miller *et al*, 2011). In Ireland, the prevalence of SIDS has fallen from an average of 2.2/1000 live births in the 1980's to 0.3/1000 live births in 2008-2010, which has been attributed to supine sleeping (Freyne *et al*, 2013). Compliance with the 'back to sleep' programme has resulted in an estimated fifty-one percent of infants spending most of the time on their backs (Losee & Mason, 2005). Although deformational plagiocephaly is not a new diagnosis, its recognition and diagnosis have been more common since the early 1990s, when the 'back to sleep' recommendation was implemented (Miller *et al*, 2011).

In the prone position, head control of a normal infant is usually acquired at one month of age and by four months of age the infant can hold its trunk off a surface on extended arms with its head erect (Argenta *et al*, 1996). The normal infant can roll from the prone to the supine position by six months of age, but it is not until approximately six to eight months of age that the infant can roll from the supine to the prone position spontaneously. Several studies have shown that children who spend little or no time in a prone position are at risk of a delay in early motor milestones when compared with infants who spend time prone (Boere-Boonekamp & van der Linden-Kuiper, 2001; Davis *et al*, 1998; Dewey *et al*, 1998; Dudek-Shriber & Zelazny, 2007; Jantz *et al*, 1997; Jennings, 2005; Majnemer & Barr, 2005; Monson *et al*, 2003; Salls *et al*, 2002), because prone positioning encourages use of upper body strength used in acquisition of many infant motor milestones. As early as 1960 Holt qualitatively reported that a small sample of prone sleeping American infants tended to crawl earlier and were more advanced in their prone motor skills than would be expected of English supine sleeping infants (Holt, 1960). Dewey *et al* (1998) found that prone sleepers had higher scores in gross motor, social skills, and overall development at six months but not at eighteen months. Although other studies have suggested that coordination of fine-motor skills may be advanced in supine sleepers (Francis-Williams & Yule, 1967), the encouragement of prone play for infants is important to maximise development of upper-body strength.

- 10.3.4 Manual therapy for DP

The most valuable instrument to avert head deformities should be early intervention for prevention, with positional advice, manual therapies and stretching exercises. The use of orthotic helmet therapy is implemented in unresolving cases. Manual therapy approaches to treatment include the use of physical therapy (van Vlimmeren *et al*, 2008), physiotherapy (Loveday & de Chalain, 2001), osteopathic medicine, (Lessard & Gagnon, 2011) and particular bedding pillows (Wilbrand *et al*, 2013). However, Bialocerkowski *et al* (2005) question the quality of clinical studies examining the effects of physiotherapy.

The RCT of Vlimmeren *et al* (2008) found that physical therapy significantly reduced the prevalence of severe deformational plagiocephaly compared with usual care, if administered by eight weeks of age. Another prospective RCT by Wilbrand *et al* (2013) found that both stretching exercises and the bedding pillow were associated with a reduction of positional head deformities when applied for six weeks.

- 10.3.5 Osteopathy for DP

DP is a problem of infantile asymmetry and, according to Sergueef *et al* (2006), the flattened occiput transforms the axes and planes of movements of the head. Other authors propose that these asymmetries of the occiput may create further postural compensations (Lessard & Gagnon, 2011). Seifert (as cited in Biedermann 2005) published data on unselected groups of newborn infants where she found that more than ten percent of them show signs of asymmetry of the functioning of the upper cervical spine. Philippi *et al* (2006b) suggest that reduced cervical spine rotation in the supine position indicates a sternocleidomastoid (SCM) muscle or upper trapezius muscle problem and/or restricted movement in the C1/C2 joint. Reduced cervical spine rotation in the prone position indicates a dysfunction of the anterior and posterior cervical muscles and/or fixation in the C2-C7 joints (Philippi *et al*, 2006b). These suggestions are supported by findings of Hutchison *et al* (2004) who propose a close connection between cervical spine mobility and the spontaneous improvement of cranial shape. They suggest either an in utero cause or a birth cause for the neck tightness. However, the numbers in this study were small, and not all infants were tested, due to non-compliance at the time of testing (Hutchison *et al*, 2004). Therefore, these results need confirming in a larger study.

In a pilot study on the effectiveness of osteopathic treatment in the treatment of DP, Lessard *et al* (2011) recommend that this treatment approach should include:

"the normalization of the skull base and particularly the strains, the optimization of vertebral alignment and normal mobility of the head/neck (without using thrust technique), the normalization of cranial membranes, cranial sutures and intraosseous lesions." (Lessard *et al*, 2011 p195).

In this study, anthropometric, plagiocephalometric and qualitative measures were administered before, during and after treatment. The results suggested that four osteopathic treatments at two week intervals contributed to the improvement of cranial asymmetries in infants younger than 6.5 months. However, because of the small sample size (n=10) and the absence of a control group, no definitive conclusions could be made that the decrease in asymmetry observed in this sample were due to the osteopathic treatment alone and a larger sample, using a RCT is needed to explore this hypothesis further.

- 10.3.6 Positional advice for DP

The association between DP and positional preference, asymmetrical positioning, and feeding positioning (Hutchison *et al*, 2004; van Vlimmeren *et al*, 2007) gives rise to the hypothesis that addressing the infant positioning patterns and motivating parents to carry out a structured programme to prevent positional preference reduces the risk of severe DP (van Vlimmeren *et al*, 2008). The increase in incidence of DP since the introduction of infant supine sleeping as a preventive measure for SIDS gives further strength to this theory. After a diagnosis of DP has been confirmed, treatment involves the combination of behaviour modification and non-invasive measures, at least in the early phases. Initially, parents should be given instructions to alternate sleeping positions and the avoidance of repetitive positioning (Saeed *et al*, 2008). As the skull grows rapidly in the first two years of life, such measures are generally found to be sufficient for self-correction of the skull if implemented early (Saeed *et al*, 2008).

Cavalier *et al* (2011) prospectively compared parental advice about SIDS prevention alone in the control group, with advice about SIDS and deformational plagiocephaly prevention in the intervention group. At four months the intervention group had thirteen percent DP compared with thirty-one percent in the control group, demonstrating a significant impact of advising parents on SIDS prevention sleep positioning but also alerting parents to the risks of DP, and providing information on strategies to help avoid this outcome (Cavalier *et al*, 2011). Other authors report similar findings, suggesting that early intervention and parent education are essential in decreasing the rate of deformational plagiocephaly (Aarnivala *et al*, 2015; Hutchison *et al*, 2010). In a RCT with healthy newborns, Aarnivala *et al* (2015) sought to evaluate the effectiveness of intervention in the newborn's environment, positioning, and handling on the prevalence of DP at three months and to investigate the causal relationship between DP and cervical imbalance. They found at three months that the prevalence of DP was lower in the intervention group in both two dimensional (11% versus 31%) and three dimensional analyses (15% versus 33%), and the asymmetry was milder in the intervention group. Infants with DP at follow-up had also developed more torticollis. The researchers in this study concluded that early parent guidance effectively reduces the prevalence and severity of DP and improves the cervical range of motion at three months, and that educating both parents and professionals about proper infant positioning on a national scale could help minimise public healthcare costs (Aarnivala *et al*, 2015).

- 10.3.7 Helmet therapy for DP

The use of orthotic helmets in cases of non-resolving DP is controversial. Some authors recommend that, in the absence of detectable satisfactory improvement of cranial shape following positional advice and/or manual therapy, orthotic helmet treatment can be effective in correcting cranial deformities (Biggs, 2003; Turk *et al*, 1996; Wilbrand *et al*, 2013). Kelly *et al* (1999) found that the greatest benefit of helmet therapy is derived when used within the first year of life. However, no clear criteria for initiation of helmet therapy have been established, there is significant cost associated with this approach and the treatment itself is not without adverse consequences (van Wijk *et al*, 2014). In consultation with health professionals, van Wijk *et al* (2014) defined side effects as skin irritation, pain, sweating, odour of the helmet, problems with accepting the helmet, and feeling hindered in cuddling because of the helmet. In a clinical report by Laughlin *et al* (2011), they recommended against using helmets for infants with mild to moderate deformities. Van Wijk *et al* (2014) conducted a single-blinded RCT to compare the risks and benefits of helmet therapy with the natural course of the condition and reported similar outcomes in eighty-four infants with moderate to severe DP between the two groups. This is supported by other authors who found no significant difference between orthotic and non-orthotic methods over a longer period of time (Loveday & de Chalain, 2001).

- 10.3.8 Untreated DP

DP is generally expected to improve with repositioning, carrying advice, cranial growth and hair camouflage. However, research suggests that without early intervention, DP does not resolve fully (Boere-Boonekamp & Linden-Kniper, 2001; Kane *et al*, 1996) and there is a risk of permanent cosmetic deformation (Budreau, 1987; Chan *et al*, 1995; Miller & Clarren, 2000). There are early reports of persistent asymmetrical faces (Lloyd-Roberts & Pilcher, 1965). Boere-Boonekamp and van der Linden-Kuiper (2001) showed twenty-five percent of 623 infant's demonstrated persistent asymmetric features after two years and Steinbok *et al* (2007) reported evidence of asymmetry five years after initial diagnosis. Chang *et al* (2001) showed that craniofacial asymmetry present at six months of age had a high probability of persisting into adolescence and early diagnosis was important to prevent possible sequelae. Others have observed details of long-term facial asymmetry such as: forehead protrusion ipsilateral to the occipital flattening, chin deviation to the side contralateral to the occiput flattening and displacement of the temporomandibular joint and ear (typically anteriorly on the side of the occiput flattening with respect to the other side) (St John *et al*, 2002). The degree of auricular displacement correlates with the severity of cranial asymmetry. Manouvrier (1883) (as cited in Captier *et al*, 2003) was the first to demonstrate that skull base asymmetry showed an asymmetric three dimensional position of the external acoustic meatus.

More concerning than the cosmetic effects of unresolved DP is the suggestion of potential negative physical and psychosocial effects into childhood (Najarian, 1999; Rekate, 1998). Children with DP are thought to be more prone to developing problems related to: postural compensations (Hylton, 1997; Moss, 1997), musculoskeletal dysfunction (Biggs, 2003), visual perception and ophthalmic dysfunction (Balan *et al*, 2002; Canale *et al*, 1982; Gupta *et al*, 2003; Rekate, 1998; Siatkowski *et al,* 2005), temporomandibular joint articulation (St. John *et al*, 2002), and developmental achievements (Kordestani *et al*, 2008; Panchal *et al*, 2001). Boere-Boonekamp & van der Linden-Kuiper (2001) estimated that 2.4 percent of all children with an initial diagnosis of DP would suffer from restricted range of motion and/or flattening of the skull along with the risk of psychomotor retardation, dysfunction of the nervous system, oro-facial developmental problems, ophthalmic dysfunction, ear, nose and throat (ENT) dysfunction and gastro-intestinal dysfunction. Yet a causal relationship between DP and brain dysfunction, including motor development disorders, has not been established (Persing, 2001).

The literature surrounding the cognitive outcomes among patients treated for DP remains scarce and ill-defined. It is suggested that school-age children with DP were more likely to require special education services in schools, including speech therapy, occupational therapy, and physical therapy (Miller & Clarren, 2000). Miller and Clarren (2000) reported that 39.7 percent children (n=63) with DP had received special educational services compared with 7.7 percent (n=91) of children in the control group (Miller & Clarren, 2000). Similarly, Steinbok *et al* (2007) reported that thirty-three percent of children with persistent DP had received learning assistance and fourteen percent were in a special class. More recently, Shamji *et al* (2012) indicated that special education was required in fifteen percent of cases with DP, which was significantly lower than the previous studies.

10.4 Craniosynostosis

Plagiocephaly may present itself as malformational or deformational. Malformational plagiocephaly involves a structural cranial base asymmetry secondary to a localised growth defect associated with premature closure of the cranial sutures (Captier *et al*, 2003). In 1851, Virchow (as cited in Argenta *et al*, 1996) was the first to introduce the term ‘craniostenosis’. This is also called plagiocephaly with synostosis or, more commonly, craniosynostosis. Secondary effects of cranial base abnormality (Moss, 1975) and secondary tensile effect of foetal head restraint (Graham *et al*, 1979) are two theories put forward for the pathogenesis of craniosynostosis. Hinton and co-workers (1984) postulated that increased tension, ischemia, or anoxia played a role in the increased proliferative activity resulting in cartilage formation and accentuated interdigitation at the sutures, causing the premature closure found in craniosynostosis.

The incidence of craniosynostosis is much lower than DP, being approximately 1/2500 births. The phenotypic characteristics of craniosynostosis are distinctive from those of DP and as the prognosis for growth and therapeutic intervention differ, it is important to distinguish between the two mechanisms. Craniosynostosis always requires medical management by an orthopaedic specialist. Previously, early surgery was commonly recommended for children with DP, based on the mistaken assumption that affected children had true craniosynostosis (Pollack *et al*, 1997). The routine use of CT-scanning, supplemented when necessary by three dimensional reconstructions, for cases in whom the patency of the lambdoidal suture was in question on plain radiographs, facilitated a more realistic assessment of the true frequency of lambdoidal synostosis (Pollack *et al*, 1997).

In a study of 102 patients, Huang *et al* (1996) noted differences in the detailed clinical and imaging features of true craniosynostosis and DP. Both groups of infants initially presented with unilateral occipitoparietal flattening and contralateral occipital bossing. However, this bossing was present mainly in the occipital region in the deformational cases and in the parietal region of the craniosynostosis cases. Huang *et al* (1996) found in DP, the ipsilateral ear was displaced anteriorly, whereas in craniosynostosis it was displaced posteriorly. Isolated single-suture craniosynostosis is associated with a three- to five-fold increase in the risk of developing speech and language deficits (Miller & Clarren, 2000) most likely associated with the structural asymmetrical features of the condition.

10.5 Congenital Muscular Torticollis (CMT)

Congenital muscular torticollis (CMT) is the third most common musculoskeletal abnormality in infants next to hip dysplasia and clubfoot. The reported incidence is 0.4 to 2.0 percent (Cheng *et al*, 2000); however, Stellwagen *et al* (2008) reported that sixteen percent of 102 normal newborns were found to have torticollis. CMT is a result of shortening or excessive contraction of the SCM muscle with limited range of motion in both rotation and lateral flexion in the neck and an imbalance in muscle function around the neck (Binder *et al*, 1987; Cheng & Au, 1994; Emery, 1994). As CMT is associated with other intrauterine positioning disorders, it is proposed that head positioning in utero can selectively injure the SCM muscle, leading to development of a compartment syndrome (Davids *et al*, 1993). Hamanishi & Tanaka (1994) found that a persistently turned foetal head towards the anterior wall of the uterus could cause shortening, disturbed venous circulation, and contracture of the SCM muscle on the side of mother's spine. In CMT, the limitations of head rotation become apparent by one week of age (Chang *et al*, 2001). Other associations have been made with breech presentation, birth trauma or forceps use during delivery (Yu *et al*, 2004). Obstetric histories of the mothers of 624 cases of infantile torticollis showed a total of 62.2% with difficult labour, breech deliveries, or caesarean section (Cheng & Au, 1994).

There is a strong association between CMT and DP for which two mechanisms have been proposed. Due to the positional preference in CMT, there is a high risk that infants will develop DP (Golden *et al*, 1999; Kalra & Walker, 2012). This contrasts with the development of torticollis as a result of ipsilateral SCM muscle shortening from a preference for head positioning (Biggs, 2003). Ohman *et al* (2009) found that DP occurred at two months of age in sixty-one percent (n=15) of infants with CMT and in forty-two percent (n=14) in a non-CMT the control group. While DP decreased significantly between two and ten months of age in both groups, at ten months of age minor DP continued in thirty-nine percent (n=22) of the CMT group but in none in the control group. A relationship between CMT and developmental dysplasia of the hip (DDH) has also been found, especially in boys. Therefore, children with CMT should be screened for DDH and infants with DDH should be carefully followed up for the development of CMT (Von Heideken *et al*, 2006).

Infants treated for CMT are encouraged to spend time in the prone position to stimulate head posture and neck strength and to reduce the risk of DP (Ohman *et al*, 2009). However, infants with CMT have somewhat low tolerance of the prone position if it is not introduced early in life, possibly because of the muscular imbalance in the neck (Ohman *et al*, 2009; Philippi *et al*, 2006b). The most common treatment is exercises to stretch the SCM muscle (Chang *et al*, 2001). If this fails, surgical release of the SCM is necessary (Chang *et al*, 2001). When torticollis is inadequately managed, infants may develop progressive limitation of cervical movement along with craniofacial asymmetry, plagiocephaly, compensatory scoliosis, delayed achievement of early motor milestones and functional asymmetry similar to hemiplegia (Binder *et al*, 1987; Cheng *et al*, 2001; Ohman *et al*, 2009; Schertz *et al,* 2008; Yu *et al*, 2004).

10.6 Measurement of Asymmetry

Asymmetrical posturing in infants may be due to neurological, mechanical or structural aetiologies, of which mechanical aetiologies are the most common (Hamanishi & Tanaka, 1994). Projection radiography or CT-scanning is required to definitively distinguish between DP and other more complex cases of cranial asymmetry, but these examinations are limited by accessibility, radiation exposure and cost. The limited research in this area reports on the use of instrumentation including goniometry, arthrodial protractor, photography and video recording (Aarnivala *et al,* 2015; Cheng *et al,* 2000; Emery, 1994; Klackenberg *et al*, 2005; Philippi *et al*, 2006a; Rahlin, 2005). Van Vlimmerman *et al* (2006) designed a non-invasive measurement instrument, known as plagiocephalometry, which uses a thermoplastic band to measure a variety of ratios related to the shape of the cranium. Plagiocephalometry, which is the only validated, easy-to-apply, method of diagnosing plagiocephaly (Ohman, 2012; van Adrichem *et al*, 2008; van Vlimmeren *et al*, 2006; Vinkers *et al*, 2013), is used to quantify asymmetry of the skull thus making it possible to study the natural course of skull asymmetries, as well as the effects of conservative treatments (van Adrichem *et al*, 2008; van Vlimmeren *et al*, 2006). The 'severity scale for assessment of plagiocephaly' (see Ohman, 2012) is regarded as useful in tracking progress made during treatment of DP (Losee & Mason, 2005) and has recently been reported to have satisfactory inter-rater reliability (Ohman, 2012). Other approaches to measurement include an asymmetric index designed with the use of a splint material (Ezeform strip) that can make a permanent ring of the head circumference (Chang *et al*, 2001) and anthropometric cranial measurements with a metal spreading calliper, which have been used in recent studies to calculate the oblique cranial length ratio (Pogliani *et al*, 2014).

The reliability of visual estimation of cervical range of motion has not been established, though visual estimation is most frequently employed when clinically assessing asymmetries including CMT, positional preference and DP (Boere-Boonekamp & van der Linden-Kuiper, 2001; Cioni *et al*, 2000; Philippi *et al*, 2004). Analyses of cervical rotation revealed that during the first four months of life, head turn is physiologically associated with a contralateral cervical lateral flexion in the supine position and an ipsilateral cervical lateral flexion in the prone position (Philippi *et al*, 2006b). Trunk convexity is the clinical counterpart of scoliosis, which is radiologically determined by the rib-vertebra angle, but radiation exposure limits the use of spine radiographs for differentiating between progressive and resolving idiopathic asymmetries (Philippi *et al*, 2006b), and they are not recommended for routine use in young infants. Thus, studies using radiograph on effectiveness of conservative, orthotic and operative interventions for asymmetries have focused on children older than one year (Diedrich *et al*, 2002; Dobbs & Weinstein, 1999, Weiss *et al*, 2003).

Treatment of cranial asymmetry is thought to be straight forward in most cases and should resolve spontaneously before the age of two years with conservative approaches such as positioning, handling, stretching exercises and some manual therapies (Lloyd-Roberts & Pilcher, 1965; Philippi *et al*, 2006a). These interventions can make a significant difference if started early (Amiel Tison 2009; Cheng & Au, 1994; Philippi *et al*, 2006a) and may prevent the secondary craniofacial deformations that are increasing in incidence (Philippi *et al* 2006a, Stellwagen *et al*, 2008). Therefore, knowledge of the presentation of symptoms is important in the clinical decision-making with regard to young infants with asymmetry and the design and validation of a useful screening instrument is recommended (Nuysink *et al*, 2008).

Due to the limitations of radiograph, asymmetry scales have been considered an alternative approach to asymmetry measurement in infancy and a variety of designs have been explored by researchers. Cioni *et al* (2000) described an asymmetry scale, which evaluated asymmetric general movements and served for early identification of hemiplegia. Boere-Boonekamp and van der Linden-Kuiper (2001) defined an infantile positional preference by evaluating the preference of head rotation to one side and restriction of head rotation to the contralateral side in the supine position. Philippi *et al* (2004) developed a measurement scale, which uses degrees of trunk convexity and cervical rotation deficit. Philippi *et al* (2006a) proposed that these parameters constitute the diagnosis of a condition they termed 'infantile postural asymmetry' and can be used to differentiate at an early stage between progressive and resolving idiopathic infantile asymmetry.

10.7 Infantile Postural Asymmetry

Infantile asymmetry pattern analysis has indicated that morphological and functional anomalies are intricately linked and that infants with one sign of asymmetry have, in fact, a more generalised disturbance (Philippi *et al,* 2006b). To date, terminology has been preliminary and a potential source of confusion. The work by Philippi and colleagues has attempted to address the issue of terminology by coining the term 'infantile postural asymmetry' (IPA) and used this to describe a complex of asymmetrical positioning in infants that includes reduced cervical rotation and/or idiopathic infantile scoliosis (Philippi *et al,* 2006a). Philippi *et al* (2004) developed a measurement scale for the diagnosis of IPA which measures the coincidence of cervical spine rotation deficit (CRD) and trunk convexity (TC). This IPA measurement scale (Philippi *et al,* 2004) was used in a small study to demonstrate a link between osteopathic treatment in the first months of life and an improvement in IPA (Philippi *et al,* 2006a).

The IPA measurement scale has been proposed by Philippi *et al* (2004) as a non-invasive method for examining, diagnosing and managing idiopathic infantile asymmetry. Four parameters are measured, trunk convexity (TC) and cervical spine rotation deficit (CRD) as reactive movements to an orienting head turn in the prone and supine positions, using gentle visual and audible stimuli to encourage movement. In the study by Philippi *et al* (2004), extended video-recording was necessary to reliably assess general movement patterns and the degree of asymmetry was assessed by five independent, trained and blinded observers using standardised video-based measurements and a six-point scale for each of the four measurement parameters. The individual scores (1-6) from the four parameters were added together to reach a total score between 4 and 24, where 4 represents full cervical rotation without trunk convexity in both positions (i.e. no observable problems) and 24 relates to convexity that cannot be resolved and limited cervical spine rotation (i.e. marked observable problems). Therefore, the higher the score, the larger the postural asymmetry.

Philippi *et al* (2006a) proposed that the asymmetry scale could be used to monitor the development of the asymmetric infant and thus enhanced the potential for evaluating the effectiveness of therapeutic interventions in treating IPA. They also suggested that by monitoring the development of the asymmetric infant using the asymmetry scale, over- or under-treatment using manual therapy such as osteopathy, could be avoided (Philippi *et al*, 2006a). Philippi and colleagues reported possible benefits of infant positioning and handling techniques for improving IPA (Philippi *et al*, 2006a) similar to studies that found improvements in DP with positional advice (Saeed *et al*, 2008; van Vlimmeren *et al*, 2008) and suggestive of the risk of post-natal moulding in both conditions. This observation is supportive of previous associations between DP and spine asymmetry (Dobbs & Weinstein, 1999; Konishi *et al,* 1986; Lloyd-Roberts & Pilcher, 1965; Wynne-Davies, 1975).

Although a relationship between asymmetry, or more specifically IPA as defined by Philippi *et al* (2006a), and unsettled infant behaviour is unknown, the authors made the observation that excessive crying was more prevalent in asymmetric infants and reported ten out of thirty-two (31%) infants (six to twelve weeks old) identified with IPA also had excessive crying as defined by Wurmser *et al* (2001). This is higher than the most commonly reported prevalence estimates of twenty to twenty-five percent for colic and unsettled infant behaviour (de Weerth *et al*, 2013; Fisher *et al*, 2011; Hemmi *et al*, 2011; Hiscock & Jordan, 2004) as discussed earlier, and may suggest that the increased rate of excessive crying was associated with the IPA findings. However, a relationship was not found between improvement of IPA and a change in crying, sleeping and mood (Philippi *et al*, 2006a). This was a small study and was limited by a lack of radiograph monitoring for gold standard comparison with this measurement scale (Philippi *et al*, 2006a); therefore, more rigorous testing is required for definitive conclusive recommendations.

10.8 Chapter summary

Relating unsettled infant behaviour to musculoskeletal disturbance and more specifically, to evidence of infantile asymmetry conditions, is complicated by a poor understanding of the underlying processes. There are many indications that musculoskeletal disturbance is a possible consequence of intrauterine constraint, birth injuries and/or postnatal positional pressure. In spite of the high incidence of unsettled infant behaviour, with no clear causal pathway, no studies have explored a possible connection between unsettled infant behaviour and musculoskeletal disturbance. One significant obstacle in researching this hypothesis is an absence of validated methodology to assess for musculoskeletal disturbance in infancy. The observation of asymmetrical posture in infancy may be regarded as evidence for the presence of musculoskeletal disturbance and offers an opportunity for measurement that is otherwise lacking. An additional problem with researching these topics is the lack of consistent terminology when describing all the processes under scrutiny.

Philippi *et al* (2006a) attempted to address the difficulties of terminology and measurement by exploring the study of infantile asymmetry. By introducing the term 'infantile postural asymmetry' (IPA) their intention was to encompass all the idiopathic non-progressive asymmetrical syndromes of infancy. Using the IPA concept, Philippi and colleagues developed a non-invasive measurement scale to assist with the diagnosis and management of IPA and to support future research in this field.

Considering the entirety of this literature review on infant behaviour, temperament measurement, osteopathic approach and asymmetry, two prominent conclusions can be drawn. Firstly, a lack of consistency in terminology makes the research of these topics cumbersome and fragmented. Attention is needed to identify specific meanings of terms referred to within publications so that accurate analysis can be achieved. More stringent classification of terminology should be stipulated when addressing the subject of unsettled infant behaviour and potential causes of abnormal crying patterns, as well as infant dysregulation and infant temperament. Similarly, though not to the same extent, care is needed when describing the different presentations of infantile asymmetry, causal pathways and management strategies so that a universal language is established for multidisciplinary appreciation. The second conclusion is the observation that, to date, the single most consistent finding in studies on infantile asymmetry disorders is that optimal handling strategies and parental advice on infant positioning yields positive results when implemented early and in a clear structured way, and that handling and positioning practices can also impact some unsettled infant behaviours. This is of particular interest in the current research study because handling and positioning of infants are key components to musculoskeletal comfort and may, therefore, be an indication of a possible association between unsettled infant behaviour and infantile postural asymmetry.

The hypothesis that there is a relationship between IPA and unsettled infant behaviour is based on the rationale that unsettled infant behaviour and pain are related. The IPA measurement tool, which measures the coincidence of trunk convexity and cervical rotation deficit, could be an indication of musculoskeletal restriction and therefore a proxy measurement of dysfunction/pain causing unsettled infant behaviour and thus proposing a positive relationship between musculoskeletal movement and unsettled infant behaviour. Philippi *et al* (2006) demonstrated an improvement in IPA after four sessions of osteopathy, and as osteopathy is a treatment of the musculoskeletal system, this could add to the theory that IPA was measuring musculoskeletal restriction. Therefore, testing the reliability and validity of the IPA measurement scale for measuring IPA was the first aim of this study, followed by investigating its relationship with unsettled behaviour in twelve- to sixteen-week-old infants.

Chapter 11 - Methods

The main themes of this study, unsettled infant behaviour and infantile postural asymmetry, are examined in the literature review in addition to the related themes of infant temperament measurement and osteopathic approach to musculoskeletal disturbance in infants, to explore common links which have not, to date, been clearly described. This chapter presents the design, method of participant recruitment, profiles of those taking part, how sample sizes were decided upon and exclusion criteria of the study. This chapter goes on to describe the materials used in the recruitment process, measurements performed during the clinical testing and the tools used for data collection. The two primary instruments involved in gathering the data, the Revised Infant Behaviour Questionnaire - short form (IBQ-Rs) and the Infantile Postural Asymmetry (IPA) measurement scale. These are described and the approach to data analysis is presented. Consideration of ethical issues particular to this research study are described. The chapter ends with a summary of the whole approach to the study.

11.1 Reviewing the literature

A literature review was conducted to assess the current state of research in four main topic areas related to this study; unsettled infant behaviour, temperament measurement, osteopathic perspective and infantile asymmetry, with the aim of identifying gaps in the current knowledge and planning a strategy including appropriate methodologies and methods. The literature review search strategy focused on peer-reviewed literature (Medline, PubMed, CINAHL and Cochrane) with search keywords and terms; unsettled infant behaviour, colic, crying, gastro-oesophageal reflux disease, cows' milk protein allergy, microbiota, infant temperament, regulatory problems, osteopathy, physiotherapy, musculoskeletal, asymmetry, posture, postural, infancy, scoliosis, torticollis, positional preference and plagiocephaly. Related publications in the references of all articles were also sourced. As far as possible the most recent relevant publications were searched. Any new studies that were published after the fieldwork had been completed, were included retrospectively in the literature review and are examined in more detail in the discussion with reference to their relevance to the findings in this study.

11.2 Design

This observational study used a quantitative cross-sectional design to investigate the relationship between unsettled infant behaviour and infantile postural asymmetry (IPA). The rationale is that IPA is a possible reflection of musculoskeletal disturbance and the IPA measurement scale may be a useful tool in determining the extent of musculoskeletal disturbance. Infant behaviour was assessed using the short form of the Revised Infant Behaviour Questionnaire (IBQ-Rs) (Gartstein & Rothbart, 2003; Putnam *et al,* 2013) which was completed by parents. IPA was assessed using the IPA measurement scale (Philippi *et al*, 2004). Data analysis tested for possible associations between IPA and IBQ-R scores.

11.3 Participant recruitment

The IBQ-Rs is validated for use in infants three to twelve months of age (Putnam *et al*, 2014) and the IPA measurement scale is validated for six- to sixteen-week-old infants (Philippi *et al*, 2004). Therefore the target age for this study was set at twelve to sixteen weeks so that both assessments could be run simultaneously. The three month routine developmental health check for infants was an ideal opportunity to capture this age group.

- 11.3.1 Sample size

As this was a new study, the strength of the possible correlation between the IPA and IBQ-Rs was unknown, therefore a conservative estimate of R^2= 0.15 (a moderate multiple correlation) was chosen. Sample size was calculated using the power calculation method of Cohen (1988). Five variables (to permit investigation of IPA together with the demographic variables of age, sex, birth weight and parity) were chosen for the multiple regression model. For a power calculation of 0.8 and a probability value for statistical significance at 0.05, a sample size of ninety-one was needed (Table 1) (Cohen, 1988).

Table 1 - Power calculation for sample size

	Effect Size		
# predictors	**Small R^2 = 0.1**	**Medium R^2 = 0.15**	**Large R^2 = 0.35**
2	481	67	30
3	547	76	34
4	599	84	38
5	645	91	42
6	686	97	45

To achieve ninety-one participants (allowing for loss of data), 300 questionnaires were distributed to parents attending the six week developmental health check with their baby. It was assumed that clinic attendance would be eighty percent and forty percent of attendees would be recruited.

Participants were recruited via three public health clinics (PHC) in the Sligo and Leitrim areas. Infants routinely attend PHC's for developmental check-ups over the first two years of life. At the six week PHC, parents of all full-term, healthy and thriving babies were informed of the study by their public health nurse (PHN) and information packs were made available within the clinic for collection. Parents who were interested in including their child in the study were invited to collect an information pack and read the parent information sheet (PIS) enclosed. The information pack also included the study questionnaire (IBQ-Rs) and consent forms which were to be filled out and returned to the researcher at the childs three month health check when the video-recording part of the study was also carried out.

- 11.3.2 Exclusion criteria

The following exclusion criteria was used in this study;

- Infants born outside 38 and 42 weeks gestation
- Infants with underlying disease requiring medical intervention
- Infants who had already received some form of manual therapy (e.g. osteopathy, chiropractic or physiotherapy), as this may have influenced results
- Infants who had had treatment for a condition of asymmetry (e.g. congenital hip dysplasia, torticollis)
- Parents without adequate English language skills to give fully informed consent or complete the questionnaire
- Lack of parental informed consent

Seventy parents consented for their baby to be included in the study. This resulted in fifty-eight data sets being included in the analysis. Twelve data sets were lost. Five video-recordings were abandoned due to non-compliance of infants. Four questionnaire forms could not be used because of inadequate completion. Two participants were removed because the parents withdrew their child. One video-recording was excluded due to poor quality and interference.

11.4 Information Pack

The information packs distributed to parents at the PHC's contained three documents;

Parent Information Sheet (PIS)

This form was an invitation to parents to volunteer their child to participate in the study. It explained the aims of the research, details of the study design, ethical considerations and contact details for further advice (Appendix 1).

Consent Form

There were two identical copies of the consent form included in the pack for signing; one to be returned to the researcher and one for the parents' retention (Appendix 2).

Revised Infant Behaviour Questionnaire – short form (IBQ-Rs)

Parents willing for their infant to participate were invited to fill out the IBQ-Rs (Putnam *et al*, 2013) before returning to their twelve week public health appointment where the video-recording element of the IPA measurement took place. A copy of the IBQ-Rs can be found in Appendix 3.

11.5 Measures

This study used the IBQ-Rs questionnaire to assess for infant behaviour and the IPA measurement scale to assess infantile asymmetry.

- 11.5.1 IBQ-Rs

The IBQ-Rs used in this study is a short form of the Revised Infant Behaviour Questionnaire (IBQ-R) (Gartstein & Rothbart, 2003). The standard IBQ-R is a well-established parent-report measure of temperament for infants. It assesses fourteen fine-grained aspects of temperament in infants between three and twelve months of age. The short form of the IBQ-R (i.e. the IBQ-Rs) is a ninety-one item questionnaire developed to reduce demands on the parent (Putnam *et al,* 2014). Over 90% of Cronbach's alphas and part–whole correlations calculated for the short form were found to be greater than 0.70. Inter-parent agreement was nearly identical to that obtained with standard IBQ–R scales, averaging 0.41 and ranging from 0.06 to 0.76. Longitudinal stability over multiple time spans, and estimated retest reliability of the short form scales, were highly similar to those of standard forms, with estimated retest reliability averaging 0.72 and ranging from 0.54 to 0.93. Convergent and predictive validity of select short form scales were comparable to, but slightly lower than, those observed for standard IBQ–R scales (Putnam *et al*, 2014).

The IBQ-Rs uses a seven point numerical scale measuring the frequency of observed behaviour. To minimise the risk of parental anxiety about whether their child's behaviour indicated an underlying problem, there was a 'does not apply' tick box on the questionnaire. IBQ-Rs forms included an explanation that due to the validation period for this questionnaire being three to twelve months and the target age for this study being twelve to sixteen weeks, there was a possibility that not all of the questions would apply to their baby. The 'does not apply' feature permitted parents the opportunity to differentiate between activities that their baby was able to do but did not demonstrate in the designated time frame from activities that their baby had not yet demonstrated at any time. The aim of this feature was to avoid scoreless questions as far as possible and was explained in the questionnaire (Please see Appendix 4 for full text).

In addition to the standard questions on the IBQ-Rs this study included demographic questions about sex, birth weight and weight at time of testing. This additional information was requested so that the hypothesis that there is any relationship between IPA and these variables could also be tested. The position of the infant in the family was requested to investigate whether this influenced the parental perception of infant behaviour.

- 11.5.2 IBQ-Rs pilot study

The IBQ-Rs questionnaire was piloted on ten families who attended the Julie Ellwood Osteopathic Clinic. Parents of infants aged twelve to sixteen weeks who attended the osteopathic clinic for private consultation agreed to trial the questionnaire and feedback their comments on the appropriateness of the document. Some minor issues were detected at this stage of the pilot as follows;

- Different approaches to asking the same question, yielded different answers.
- Two opposing questions with contradictory responses.
- Some difficulty in the interpretation of questions possibly due to different care-giving environments.
- Questions unanswered, presumably because they were not understood.
- Although the short form of the revised IBQ was chosen, this still took 30 minutes to complete. Of concern was that with time constraints on parents of young babies and lack of sleep during this period, a 30 minute questionnaire could be quite demanding.
- It was acknowledged that the socio-economic group captured through the private osteopathic clinic may not be representative of the local public health population and therefore the generalizability of the pilot data could be limited.

The IBQ-Rs questionnaire was scored using the IBQ-Rs scoring sheet (Appendix 5). Although some issues were detected in the responses, these were regarded as minor and affected a small proportion of the questionnaire. The pilot data targeted infants through the private clinic, however the main study would recruit infants through PHC's thus addressing generalizability limitations of the pilot. Overall the quality of the responses to the IBQ-Rs were satisfactory and the questionnaire was regarded as appropriate for the study.

- 11.5.3 Infantile Postural Asymmetry measurement (IPA)

The IPA measurement scale (Philippi *et al,* 2004) is a clinical method used to describe and quantify infantile postural asymmetry (IPA). It uses a six-point numerical scale in four categories, trunk convexity (TC) and cervical spine rotation deficit (CRD), in the prone and supine positions. For each item, 'trunk convexity supine', 'trunk convexity prone', 'cervical rotation deficit supine' and 'cervical rotation deficit prone', scores range from 1-6 following the precise descriptions of Philippi *et al* (2004) for the IPA scale (Appendix 6). As many asymmetric movement patterns disappear spontaneously during the first six weeks of life (Lloyds-Roberts & Pilcher, 1965), and after sixteen weeks voluntary movements may mask underlying asymmetry, this instrument is validated for infants between six and sixteen weeks.

Psychometric analysis of the IPA measurement scale indicated good reliability and consistency of the testing method with an intraclass correlation coefficient of 91.5 percent and Cronbach alpha 0.84. A 95 percent confidence interval of 86.0–97.0 percent reflected a very good inter-observer reliability. The interpretation is that 91.5 percent of the variance in the scores results from true variance among the asymmetric infants. The contribution of the observer variance to the total variance of the score was 0.6 percent with a 95 percent confidence interval of 0.0 to 2.0 percent. Moreover, a Cronbach's alpha of 0.84 signifies a high internal consistency of the items without redundancy.

- 11.5.4 IPA measurement scale pilot study

The IPA measurement procedure was piloted on ten infants who attended the Julie Ellwood Osteopathy Clinic, without the use of video-recording. This was done to familiarise the researcher with the procedures involved and to highlight areas of the process that require increased attention to ensure the smooth operating processes. While no recording was performed, the field of view was assessed and regarded as too far from the test mat at two metres (Philippi *et al,* 2004). Therefore the distance of the video camera was altered from two metres to one metre to achieve the same field of view. No other issues were raised.

11.6 Equipment

- 11.6.1 IPA measurement mat

The sterile mat on which the infants were placed for the IPA video-recording measured 60cm x 90cm and was black in colour. A straight white line marked centrally along the length of the mat divided it equally. A second straight line was marked perpendicular to the first 30cm from the top of the mat (Appendix 7a). The mat was kept warm by placing a warm (not hot) water bottle onto it for a couple of minutes prior to each test. The mat was cleaned with a skin sensitive sterile solution between each test.

- 11.6.2 Video-recording

The video camera was positioned on a stand above the mat at a distance of one metre. This achieved the same field of view as the original study by Philippi *et al* (2004) which validated the recording at a distance of two metres. Video-recording was performed using the iPhone 4s digital camcorder – 8-megapixel iSight camera and video recording, HD (1080p) up to thirty frames per second with audio. This device was chosen because of its ease of set-up, fast image transfer and portability. It was mounted securely onto the stand (at one metre distance) (Appendix 7b and

7c) using an iPhone 4s gripper attachment and controlled remotely with 97cm cable attachment.

- 11.6.3 Video-editing

Video-editing was carried out by the researcher using Movavi software (www.movavi.com) on a HP laptop where images were stored in password protected and encrypted software called TrueCrypt (version 7.1a) (www.truecrypt.org/downloads*)*.

11.7 Procedure

Parents who consented to the study were invited to bring their baby to the video room following their twelve week developmental health check where the video recording process was fully explained. The completed consent and IBQ-Rs forms were collected. A unique identification number was assigned and placed on all forms. The questionnaires were stored securely until a later date when they were scored by the researcher using the IBQ-Rs – score sheet (Appendix 5).

The room was kept at 21 – 23ºC, monitored by a portable thermometer. The environment was quiet and the light intensity was uniform and moderate. The card with the assigned unique identification number (already allocated to the IBQ-Rs) was placed in the top right hand corner of the mat, within view of video camera shot. The researcher and parents were positioned behind the camera. The babies were undressed by their parent and once they had reached a state of active wakefulness without crying they were placed on the warmed test mat by a parent.

The researcher gently aligned the baby onto the central cross marking on the mat and started the test process which took no more than five minutes from start to finish. Recording of the spontaneous and reactive movements was started with the infant's head held shortly in the middle supine position. For the next 60 seconds the spontaneous movements were recorded. Then a head turn was induced by presenting noises, toys, or the researcher's face, and moving them from one side to the other. After at least two turns to each side, the infant was turned onto their front by a parent and the head was held shortly in the middle prone position. The same procedures were repeated.

Once this was completed the parent was asked to lift the baby from the test mat and return clothing. At the same time the researcher checked the recording to ensure the image was clear and the ID sticker was visible. The researcher then transferred the recording onto password protected encrypted software and deleted the recording from the camera. Parents were encouraged to contact the researcher over the following weeks if they had any new concerns or questions with regard to the study.

A convenience sample of five independent observers were recruited to analyse and score the video data for the IPA scale. All were General Osteopathic Council (GOsC) Registered Osteopaths and Criminal Records Bureau (CRB) checked. They were recruited using invitation letters to osteopaths in Ireland and the UK who had a minimum of ten years of experience treating infants. The observers were provided with a presentation of the study aims and training on the use of the IPA scale, by the researcher. Each video-recording was read by at least three different observers, at different times and locations, to reduce risk of bias. All IPA score sheets were collected and stored until later scoring and analysis.

11.8 Measurement scoring

The video recordings were analysed using the IPA measurement scale (Appendix 6). For each analysis, individual scores were provided for CRD and TC in the supine and prone positions by the trained independent observers. The four individual scores were recorded on an IPA score sheet and later input into an Excel spreadsheet prior to importing into SPSS for analysis. This was completed three times, by three separate observers, for each video-recording. IBM SPSS Version 22 was used for all data analysis (IBM Corp., 2013).

The IBQ-Rs forms were transcribed into an Excel spreadsheet and scored using the corresponding IBQ-Rs score sheet (Appendix 5). All other analysis was carried out using SPSS (Version 22) software. Results of analyses are detailed in Chapter 12.

11.9 Ethics

It was acknowledged early in the planning of this research study that the research design which involved video-recording was highly sensitive. The study participants, being infants, were a particularly vulnerable group. The parents of the infants were also vulnerable due to the demands that early parenting can place on individuals. Therefore ethical considerations required rigorous attention. Ethical approval for this study was obtained from the British School of Osteopathy, University of Bedfordshire, Adelaide and Meath National Children's Hospital and Sligo General Hospital. The ethical approval was obtained based on adherence to several guidelines within the study.

- 11.9.1 Information on study

The PIS gave detailed information to the parents of participating babies so they were clear about the rationale for the study, with instructions of the babies' involvement and the right to decline their babies' participation in the study without any detriment to themselves or their babies (Appendix 1). Details of the consent form and IBQ-Rs were introduced in the PIS. Completed consent and IBQ-Rs forms were collected from willing parents of babies at their routine twelve week developmental appointment.

- 11.9.2. Informed Consent

The consent form (Appendix 2) clearly defined what parents were consenting to and that a decision to decline participation would have no effect on the care of their baby. Also, a change of mind and decision to withdraw was permissible at any stage in the study without question or detriment. Parents were informed of their right to access the results of the overall study once completed and provided the researchers with their email address as a source of contact should they be interested.

- 11.9.3 Participant anonymity

Each participant was assigned an identification code as soon as informed consent was obtained and participation in the study was agreed. The IBQ-Rs form (Appendix 3) was labelled only with the ID number. This number was also placed on a card in view with the baby while the videotaping was taking place. There was no requirement for personal information to be attached to either the IBQ-Rs forms or video analysis once the ID number had been assigned.

Signed consent forms were also labelled with the unique identifying number and were stored inside sealed brown envelopes and locked in a filing cabinet at the researcher's office. IBQ-Rs forms were also securely stored until scoring was performed using the IBQ-Rs score sheets by the researcher (Appendix 5).

- 11.9.4 Password protected encrypted software

The study was observational; there was no intervention to the participants. However, there was a need to undress the baby for the short video recording as anatomical landmarks played a crucial role in assessing the movements and posture of the baby and this was explained in the PIS (Appendix 1). The baby's genitalia was obscured at all times during the video-recording with the use of a sterile napkin. The images were immediately transferred from the camera onto TrueCrypt password protected and encrypted software, to which only the researcher had access (www.truecrypt.org/downloads*)*. The images were then anonymised by the researcher by blocking out the eyes. All original images were deleted. Only the researcher had access to the images.

Analysis of the images by five trained observers was performed in the presence of the researcher who gave access to the images on the password protected software. Once images were analysed, the software was locked immediately after use. The identification of the images was by identification code given to them at the time of recording and visible on an ID card in the screen shot of each recording.

- 11.9.5 Participant withdrawal

At all stages it was made clear to the parents that withdrawal of their child from the study was permitted without detriment, even after informed consent had been given and if images had already been taken these would be deleted without delay. Parents were encouraged to speak with the researcher at any stage in the process should there be any questions or concerns. This information was detailed on the PIS (Appendix 1).

- 11.9.6 Data storage

At the end of the study data will be stored securely at the BSO for a period of six years, after which time electronic data will be deleted and paper data will be shredded.

11.10 Chapter summary

The overarching approach of this study involved two methodological data collection processes. The behaviour of infants was examined for evidence of unsettledness by using the IBQ-Rs and the results of this parent-report form were scored using the IBQ-Rs score sheet. The infants were separately assessed for signs of asymmetrical movements and posture using the IPA measurement scale which required the video-recording of movement patterns and spontaneous responses to stimuli. This assessment of asymmetry in infants was selected as an indicator of musculoskeletal disturbance, which is of particular interest to osteopaths who treat infants with unsettled behaviour. Any relationship between unsettled infant behaviour, as identified using the IBQ-Rs, and infantile asymmetry, as measured using the IPA scale, may also suggest a relationship between unsettled behaviour and musculoskeletal disturbance and would enhance the possibilities of further research in this field.

Chapter 12 – Data Analysis

Researching the question of whether there is a relationship between unsettled infant behaviour and infantile postural asymmetry was the focus throughout the data analysis. The study design resulted in a lot of data and indicators of possible trends were lacking due to a paucity of research in the area of infantile postural asymmetry and unsettled behaviour.

Fifty-eight IBQ-Rs forms had ninety-one questions, each with nine possible scores (1-7, NA and blank). These were calculated using the IBQ-Rs score sheet to produce fourteen behaviour subsets and three main constructs, surgency/extraversion (SUR), negative affectivity (NEG) and orienting/regulation (REG), as previously described for each participant.

The IPA measurement scale for the fifty-eight participants was analysed three times. Each of the three analysis produced five sets of results (Supine CRD, Prone CRD, Supine TC, Prone TC and Total IPA score). Within these groups it was also interesting to analyse the scores based on CRD only and TC only outcomes. The raw data for the patient demographics, IBQ-Rs results and the IPA measurement scale results are located in the appendices.

This chapter starts with a summary of the baseline demographics for the fifty-eight infants included in the study. The inter-rater reliability results for the three IPA scores among the five observers are presented. Preliminary analysis, including multiple regression, ANOVA and MANOVA studies, are reported. Where interactions are identified, these are further explored to examine what is driving these interactions. This chapter ends with a summary of the main findings in the data analysis which are then discussed in detail in Chapter 13.

12.1 Baseline demographics

Three hundred questionnaire packs were distributed to the parents of infants attending their six week public health check clinic. Of these, the parents of seventy babies consented to participate in the study. Twelve data sets were rejected due to problems with video-recording, incomplete questionnaires or withdrawal.

The baseline characteristics of the remaining fifty-eight infants for gender, birth rank and weight were calculated. All fifty-eight participants were aged between twelve and sixteen weeks as per study inclusion criteria; nineteen were female (33%), twenty-five were first born (43%), thirteen were second born (22%), seventeen were third born (29%) and three were fourth born (5%). The birth weight of infants ranged from 2.24kg to 4.48kg (mean = 3.52kg). All infants weighed between 4.08kg and 7.71kg (average weight was 6.4kg) by 12-16 weeks of age. See Table 2 for a summary of the IBQ-Rs patient demographics. The raw data for patient demographics can be found in Appendix 8.

Table 2 - Participant demographics summary

	Age (weeks)	Birth weight (kg)	Current weight (kg)	Position in family
Mean	**14**	**3.52**	**6.40**	**N/A**
Median	**14**	**3.51**	**6.56**	**2**
Minimum	**12**	**2.24**	**4.08**	**1**
Maximum	**16**	**4.48**	**7.71**	**4**
Standard Deviation	**1.07**	**0.47**	**0.75**	**N/A**
Interquartile Range	**1.25**	**0.75**	**0.81**	**2**

12.2 IPA data

The IPA score involved the measurement of four parameters, cervical spine rotation deficit (CRD) supine; CRD prone; trunk convexity (TC) supine and TC prone. Five independent osteopaths were employed to read the IPA scores and each score was read three times. The raw data for the IPA individual scores and mean scores across three readings can be found in Appendix 9.

12.3 IBQ-Rs data

IBQ-Rs forms were analysed using the IBQ-Rs score sheet (Appendix 5) and SPSS (version 22). Not including the additional demographic information (Appendix 8) on the IBQ-Rs forms, each questionnaire had 91 infant behaviour questions. The raw data for the IBQ-Rs subsets can be found in Appendix 10, and IBQ-Rs broad scales in Appendix 11.

Out of the possible 5,897 IBQ-Rs scores (i.e. 91 x 58), 619 (10.5%) ticked the ‘does not apply’ box. Of the ‘does not apply’ responses, 23% were connected to four IBQ-Rs questions. These were IBQ-Rs 5 ‘how often did your baby look at pictures in books and/or magazines for 5 minutes or longer at a time?’ which had a 33% ‘does not apply’ rate (22/58); IBQ-Rs 11, ‘how often did your baby smile or laugh after accomplishing something (e.g. stacking blocks, etc.)?’ had a 64% ‘does not apply’ rate (37/58); IBQ-Rs 29, ‘how often did your baby notice the sound of an aeroplane passing overhead?’ had a 59% rate (34/58); and IBQ-Rs 30 ‘how often did your baby notice a bird or squirrel up a tree?’ had a 81% rate (47/58).

12.4 Correlation and regression analyses

The hypothesis that unsettled infant behaviour is associated with postural asymmetry was tested using correlation and regression analyses.

Visual inspection of the histograms for the 3 IBQ subscales, SUR, NEG and REG, suggested they were normally distributed and this was confirmed by Shapiro-Wilk tests (*p*s > 0.05) and z values for skewness and kurtosis (-2 < *z*s < 2). Visual inspection of the histograms for the total IPA score and the 4 components suggested problems of skewness and this was confirmed by Shapiro-Wilk tests (*p*s < 0.05) and z values for skewness and kurtosis (-2 > *z*s > 2) for all except Prone CRD (Shapiro-Wilk = 0.96, p = 0.055, z skewness = -0.70, z kurtosis = -1.20). All correlation tests were therefore Spearman's rank correlations except for those with Prone CRD.

Table 3 - Correlations between IBQ-Rs and IPA scores

	Total Supine TC	Total Supine CRD	Total Prone TC	Total Prone CRD	Total IPA
SUR	0.143 (0.284)	-0.036 (0.79)	0.076 (0.571)	-0.023 (0.866)	0.061 (0.651)
NEG	0.005 (0.97)	0.088 (0.51)	0.036 (0.789)	0.023 (0.866)	0.058 (0.665)
REG	0.159 (0.233)	-0.044 (0.743)	0.129 (0.336)	0.03 (0.821)	0.127 (0.342)

TC – trunk convexity; CRD – cervical rotation deficit; IPA – infantile postural asymmetry; SUR – surgency/extraversion; NEG – negative affectivity; REG – regulation/orienting. Coefficient, p value in parentheses.

There were no significant correlations between the total and any of the four parameters of the IPA scores with the total or any subscale of the IBQ-Rs (all ps > 0.05) (Table 3).

To assess whether the relationship between postural asymmetry and unsettled behaviour might be moderated by demographic variables a series of multiple linear regressions were conducted. Standard linear regression in which all the predictors are fitted simultaneously was used. The dependent variables were the SUR, REG and NEG subscales of the IBQ-Rs. For each subscale, models were fitted with the predictors the age of the infant in weeks, sex (coded dichotomously) and either birth weight in kilograms or weight at time of testing (aged 12-16 weeks). The final predictor was one of the IPA components. Regression ANOVAs for all analyses were not significant. There was no evidence an association between IPA scores and IBQ-Rs scores nor any evidence of moderation of an association by demographic variables.

12.5 Interrater reliability

Intraclass correlation coefficients (ICC) were calculated for the IPA ratings to provide information on how well the five raters' readings correlate. A one-way model using single measures was used. A one-way model was appropriate as there were five raters and each study participant was rated by a subset of three of the raters. Single measures were used as a key aspect of the current study for testing the generalizability of the IPA ratings; i.e. single measures ICC were used to test whether the rating from a single observer in a future study would be reliable. ICC's below 0.40 were regarded as poor, 0.40 to 0.59 as fair and above 0.60 as good (Cicchetti & Sparrow, 1981). See Table 4 for the ICC results of the IPA readings.

Table 4 - Intraclass correlation coefficients for the ratings

Trunk convexity, supine position		
	ICC	**95% CI**
Single Measures	0.385	(0.22-0.55)

Cervical spine rotation deficit, supine position		
	ICC	**95% CI**
Single Measures	0.701	(0.58-0.80)

Trunk convexity, prone position		
	ICC	**95% CI**
Single Measures	0.320	(0.16-0.49)

Cervical spine rotation deficit, prone position		
	ICC	**95% CI**
Single Measures	0.738	(0.63-0.83)

The cervical spine rotation deficit ratings have acceptable reliability (ICC $\geq$ 0.7) (Landis & Koch, 1977). The trunk convexity ratings, in prone and supine position, have low reliability being both < 0.4. ICC $\geq$ 0.7 is generally considered necessary to justify aggregation of ratings data (Dixon & Cunningham, 2006), therefore summing the trunk convexity data across the five raters is not justified, as there is insufficient reliability in the ratings.

12.6 Comparisons of IBQ scores for high/low CRD

Various methods were used to split the data into two or three groups. A few analyses produced significant results but these appeared to be unstable. Very minor changes to the criterion for splitting the data would lead to effects becoming not significant.

The correlations between IPA ratings and the subscales of the IBQ were not significant. As ICCs for only cervical spine rotation were adequate for summation, it was decided to dichotomise the summed cervical spine rotation IPA ratings. A median split was used to divide the data into high and low cervical spine rotation and a series of t-tests were carried out to compare the IBQ subscales between the groups. There were no significant differences between the groups (*p*s > 0.05).

Four other dichotomisation strategies were also tried but again, no significant differences were found between high and low cervical spine rotation groups (*p*s > 0.05).

Additional variants of the dichotomisation were also carried out based on a median split of the supine rating, a median split of the prone rating and a split based on having ratings being greater than medians for both supine and prone. (e.g. Group 1 - Cervical spine rotation score was greater than median for supine (med=6) and greater than median for prone (med=12) [n=23]; Group 2 - Cervical spine rotation score was less than median for supine (med=6) and less than median for prone (med=12) [n=35]).

Another three level split was also carried out (for low, medium and high total cervical spine rotation score) and the IBQ-Rs subscales were compared. Analyses of these data showed similar findings to the dichotomisation. Analysis of using the three level split was found to be unreliable. Depending on the method used to split the data, whereby numbers per level changed by one or two items, highly variable results were found (Note, as there were 3 levels, analyses were analyses of variance).

12.7 Analyses of variance (ANOVA)

Descriptive statistics suggested an influence of sex on IBQ scores (Table 5). A series of analyses of variance were carried out with sex (male/female) and dichotomised IPA score (high/low) as the independent variables and each of the IBQ subscales as dependent variables.

Table 5 - IPA scores by Sex

	Female		Male	
	Mean	**95% CI**	**Mean**	**95% CI**
SUR	4.4	(4.0-4.8)	4.2	(3.9-4.4)
NEG	3.4	(3.0-3.7)	2.9	(2.6-3.1)
REG	5.4	(5.1-5.7)	5.2	(5.0-5.4)

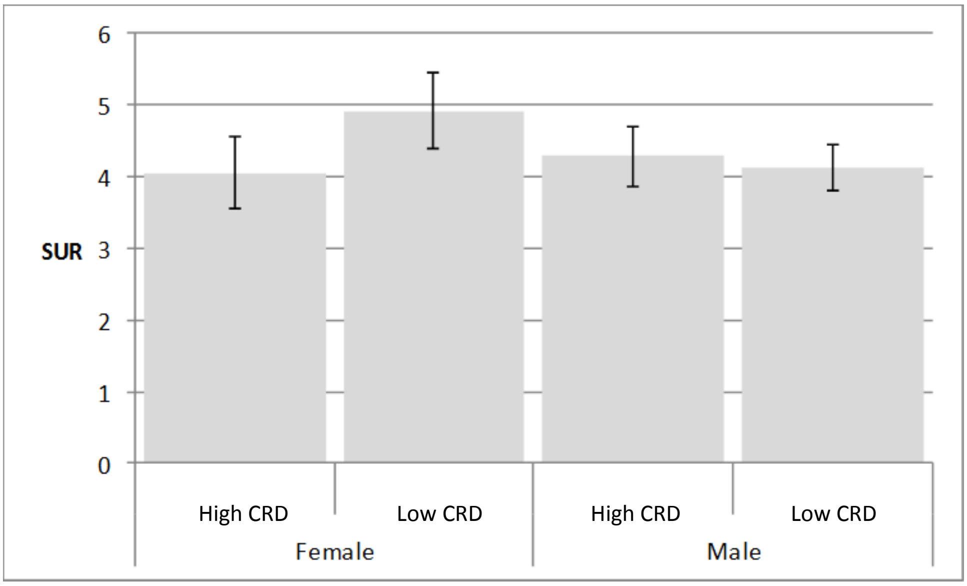
Groups were based on median split of total cervical spine rotation scores.

- 12.7.1 Results for SUR

There was no main effect of Sex, $F(1,53) = 1.5$, $p = 0.223$. There was no main effect of Group, $F(1,53) = 2.5$, $p = 0.123$. There was a significant interaction of Sex and Group, $F(1,53) = 5.2$, $p = 0.027$ (Figure 1). The effect size for this result was small, $\eta_p^2 = 0.089$ (Cohen, 1988; Miles & Shevlin, 2001). Post-hoc tests showed that for females, SUR scores were significantly higher for the low cervical spine rotation group ($\bar{x}$=4.92) than for the high cervical spine rotation ($\bar{x}$=4.05), $t(17) = -2.3$, $p = 0.038$. For males, there was no significant difference in SUR scores, $t(36) < 1$.

Note: There was an error in sex coding of one of the 58 participants. There were 38 males and 19 females in the data. There was a missing value for one baby.

Figure 1 - Interaction of Sex and Group



- 12.7.2 Results for NEG

There was a main effect of Sex, $F(1,53) = 4.5$, $p = 0.039$. Males ($\bar{x}$=2.9) had lower scores than females ($\bar{x}$=3.4). The effect size for this result is small, $\eta_p^2 = 0.078$ (Cohen, 1988; Miles & Shevlin, 2001). There was no main effect of Group, $F(1,53) < 1$. There was no interaction of Sex and Group, $F(1,53) = 2.6$, $p = 0.116$.

- 12.7.3 Results for REG

There was no main effect of Sex, $F(1,53) < 1$. There was no main effect of Group, $F(1,53) < 1$. There was no interaction of Sex and Group, $F(1,53) < 1$.

12.8 Chapter summary

An association between unsettled behaviour and musculoskeletal dysfunction is not detectable in 12-16 week old babies using IPA score. The IBQ-Rs may not be a particularly good measure of infant behaviour for 12-16 week old infants. A high proportion of questions (10.5%) in the IBQ-Rs attracted ‘does not apply’ response, with IBQ-Rs 11 (37/58) and IBQ-Rs 30 (47/58) being most affected.

Chapter 13 - Discussion

Evidence for the effectiveness of osteopathic treatment of children is currently weak. In osteopathic clinical practice, the observation of asymmetric features is one indicator of possible musculoskeletal dysfunction (Cerritelli *et al*, 2013). Links have been proposed between in-utero positioning and infantile asymmetry (Boere-Boonekamp & van der Linden-Kuiper 2001; Philippi *et al*, 2006b); between birth trauma and infantile asymmetry (Miller *et al*, 2013); between birth trauma and musculoskeletal injury (Mavrogenis *et al*, 2011; Miller *et al*, 2013; O'Mahoney *et al*, 2010; Sauber-Schatz *et al*, 2010; Van Rijn *et al*, 2009); and between birth trauma and unsettled behaviour in babies (Hipperson, 2004). While a relationship between musculoskeletal dysfunction and unsettled infant behaviour has been considered (Biedermann, 2005; Hipperson, 2004; Kotzampaltiris *et al*, 2009; Lim, 2006; Soltis, 2004), evidence for a causal association has yet to be established. Although unsettled behaviour with 'colicky' crying is seldom caused by disease, it is valuable to acknowledge the severity and importance of the stress that parents experience and how disruptive the crying is to family life (Fleisher & Barr, 2008).

The infantile postural asymmetry (IPA) scale by Philippi *et al* (2004), which measured parameters of posture and movements of the cervical and thoracic spines in infants, was used to demonstrate a reduction in asymmetric features following osteopathic treatment (Philippi *et al*, 2006a). Since a musculoskeletal therapy treated the asymmetry successfully, it can be considered a fairly strong indication that a musculoskeletal component is at least partly responsible for the asymmetry and has, therefore, provided evidence of a potential association between musculoskeletal dysfunction and the treatment of babies with osteopathy. The current study was designed to investigate whether a relationship existed between musculoskeletal dysfunction using the IPA measurement scale and unsettled infant behaviour, and to better understand the mechanisms behind both conditions. The aims of this study were; to investigate the reliability and validity of the Philippi *et al* (2004) IPA measurement scale for measuring asymmetry; to establish whether there was a relationship between IPA and unsettled behaviour in infants as measured on the Revised Infant Behavior Questionnaire – short form (IBQ-Rs) (Putnam *et al*, 2014); and to investigate whether any relationship between IPA and unsettled behaviour was mediated by, or confounded with, the demographic and developmental variables of age, sex, birth weight and weight gain in twelve- to sixteen-week-old infants.

In this study no association between unsettled behaviour and musculoskeletal dysfunction was found in twelve- to sixteen-week-old infants using the IPA measurement scale. The reliability of assessment of cervical spine rotation deficit in prone and supine positions was found to be acceptable, however the trunk convexity assessments were not found to be reliable. In addition, the IBQ-Rs may not be suitable for the measurement of behaviour in twelve- to sixteen-week-old infants as some behaviours that the questionnaire addressed appeared to not yet be exhibited by the children. The findings of the current study challenge the proposal that there is a relationship between postural asymmetry and unsettled behaviour in twelve- to sixteen-week-old infants.

.

13.1 General Discussion

The tools used in this investigation, i.e. the infant behaviour questionnaire and asymmetry measurement scale, were chosen based on their suitability to the research question and target study group. A sample of fifty-eight infants were recruited from the normal population through routine health check appointments. The challenges of recruiting large samples of infants into such studies due to ethical considerations is acknowledged. However, a larger sample was recruited in the current study than in the three previous Philippi studies (2004; 2006a; 2006b). In the current study forty-three percent (25/58) of the infants were first born babies in the family which reflects the findings of St James-Roberts and Halil (1991) that mothers of firstborns were most likely to seek support for their babies.

In the analysis of IPA data, the trunk convexity (TC) ratings were found to have low inter-observer reliability in both prone and supine positions and cervical rotation deficit (CRD) was the only reliable parameter. CRD and TC both demonstrated good internal consistency and inter-observer reliability in three previous studies by Philippi *et al* (2004; 2006a; 2006b). Because a measure cannot be valid without being reliable, the TC ratings were excluded from further analysis (e.g. Lucas & Bogduk, 2011) in this study.

Unreliable tests are problematic particularly if they are being used to form a diagnosis, treatment protocols and prognosis (Lucas & Bogduk, 2011). Factors which can affect reliability need to be identified. There are a number of possible reasons for the difference in reliability between the current study and previous research by Philippi and colleagues. The IPA scale was developed for use by osteopaths experienced in working with infants. However, this study was the first to test the IPA scale outside the original research site and it is possible that the higher reliability found in the Philippi studies may be associated with familiarity with using the measurement scales in the research setting. To be clinically useful, the results of a study must have external validity (i.e. must be relevant to a definable group of patients in a particular clinical setting) (Rothwell, 2005). This study challenges the reliability of TC in the IPA scale when tested in a clinical setting.

Unless the IPA scale can be employed as a measurement tool in clinical settings with relative ease, and maintain reliable readings that can be cross-referenced between practitioners, then widespread implementation is not valid. Lack of consideration of external validity is a recognised explanation for the underuse in routine practice of protocols that were beneficial in trials (Rothwell, 2005). Examining the concept that more IPA training may improve reliability should be regarded with caution. Lucas and Bogduk (2011) indicate that if a study group are highly selected, or if the examiners are experts with intense training, then this may reduce the likelihood that typical practitioners will perform at the same level of reliability. Although more intense training may improve the inter-observer reliability of the TC readings, the validation of an asymmetry scale using only the CRD parameter should also be considered.

Incorrect interpretation of the IPA readings may give poor results, and it is not the test that is unreliable *per se*, but error associated with variation in the interpretation of test results by examiners. The four parameters of the IPA scale rely on visual interpretation for scoring 1-6 for each parameter. Visually assessing the continual movement patterns of infants requires experience and focus to detect small differences in degrees of movement and rotation. Philippi and colleagues (2006b) propose a possible interaction between the parameters which characterise IPA depending on prone and supine positioning that, as a collective, would result in higher inter-observer reliability for the entire IPA score. This is suggestive of a problem of construct validity; i.e. TC ratings are affected by the degree of CRD which in turn is influenced by postural changes depending on the supine or prone position. Therefore, any variation in the scoring of individual parameters may be neutralised across the four parameters for the entire IPA spectrum. As the TC ratings may be influenced by both the CRD and the prone/supine positioning, it may be an explanation for TC ratings being less reliable than CRD in this study. The most parsimonious solution to the possible problem of interactions between the measures would be to remove the TC ratings.

It is also possible that there are important aspects of asymmetry that are not captured by the IPA. Philippi *et al* (2004) initially examined five potential parameters but rejected 'cervical lateral flexion' and 'oblique trunk position' due to inconsistent findings, while 'preferential head position' was regarded as unnecessary as it produced similar results to CRD. Cioni *et al* (2000) developed an asymmetry score based on eleven criteria to measure preferential movement patterns in the development of infantile hemiplegia that included head and trunk movements. Like the IPA scale, the Cioni *et al* measurement utilised an asymmetry scoring system which can assist in disease monitoring and management. However, this measurement has not been assessed for use with other populations than hemiplegic infants. A common feature of both scales was that they could be scored retrospectively from video recordings permitting assessment of intra- and inter-rater reliability (Cioni *et al*, 2000; Philippi *et al*, 2004). Boere-Boonekamp and van der Linden-Kuiper (2001) used a dichotomous measurement of cervical spine rotation to assess whether infants showed positional preference (e.g. present versus absent). However, the absence of a measurement scale for graded continuum meant the degree of asymmetric movement could not be reported. Similar to Philippi *et al* (2006b), the broad clinical spectrum of asymmetry (e.g. scoliosis, torticollis, plagiocephaly) was also examined by Boere-Boonekamp & van der Linden-Kuiper (2001). These studies highlight that for evaluation of the asymmetric infant and its sequelaes (persistent scoliosis, restricted head movements, asymmetric gait disturbances, facial scoliosis with temporomandibular joint displacement and/or functional lateralities), factors other than CRD need to be considered (Boere-Boonekamp & van der Linden-Kuiper, 2001; Philippi *et al*, 2006b), although the current study suggests that visual assessment of asymmetry may be unreliable.

The accuracy of any method of diagnosis is assessed by means of comparison to the 'gold standard', also referred to as the reference standard (Lucas & Bogduk, 2011). However, for the IPA scale this would require comparison to radiography. Computer tomography and MRI are also used but sedation is required in infants (Philippi *et al*, 2004) due to the continual movement patterns that are present in all normal six- to twenty-week-old infants (Cioni *et al*, 2000). Equally, surface topography and laser scanned three dimensional torso topography rely on cooperation to minimise postural sway and so are not suitable for infants and toddlers (Oxborrow, 2000). As the current study found no evidence that IPA is associated with unsettled behaviour, exposure to radiographs, computer tomography and MRI is not warranted.

The remaining analysis depended on the CRD results only whereas the entire IPA scale was used in previous studies. A number of different methods were used to assess the relationship between the CRD scores and the fourteen IBQ-Rs subsets, as well as the three broad components (SUR, NEG and REG), but no association between infant behaviour and musculoskeletal dysfunction using IBQ-Rs and CRD was found. This is in contrast to several publications that associate unsettled infant behaviour with cervical spine dysfunction (Hipperson, 2004; Hughes & Bolton, 2002; Olafsdottir *et al*, 2001; Soltis, 2004; Wilberg *et al*, 1999). The current study also challenges previous reports that unsettled infant behaviour resolved when a fixed lateral bend of the spine was treated with manual therapy (Biedermann 2005; Hipperson, 2004). Previous reports on musculoskeletal associations with unsettled behaviour have limitations, such as small and poorly defined sample groups and a lack of blinding (Hughes & Bolton, 2002). Unlike the current study, which used the IBQ-Rs to measure infant behaviour, previous studies relied on parental perceptions of behaviour, which are recognised to be unreliable (McGrath *et al*, 2008).

There were no significant differences in IBQ-Rs scores between dichotomised high and low CRD groups. Moreover, the absence of a relationship between sex (male/female) and the CRD high/low groups in this study is in contrast to previous findings which reported that boys were more likely than girls to present with a positional preference (Boere-Boonekamp & van der Linden-Kuiper, 2001) and with a right-sided preponderance to deformational plagiocephaly (Shamji *et al*, 2012). Therefore, this would suggest that factors other than just CRD are implicated in the presentation of deformational plagiocephaly and positional preference, and increases the argument for validating parameters in addition to CRD in future asymmetry scales.

The dichotomisation used by Philippi *et al* (2006a) included the TC and CRD parameters and by selecting the cut-off value of 12 for 'asymmetric' participants, i.e. those with a score greater than/equal to 12, an improvement in IPA score following osteopathic treatment was found. The treating osteopaths in this RCT were unblinded and the claim that the difference between osteopathic treatment and sham treatment was unrecognizable to parents is difficult to prove (Philippi *et al*, 2006a). It is unclear if the benefits associated with osteopathic treatment are related to other elements such as range of motion activities or time spent interacting with patients, which may represent placebo effects (Licciardone *et al*, 2003). There is a need to investigate the effect from general counselling and support, by placebo controlled and blinded studies, in order to document whether specific treatment regimens are effective or not (Olafsdottir, 1999).

Problems of bias with unblinded assessors, analysts and in-house observers are recognised in RCT's (Holman *et al*, 2015). Multiple lines of evidence suggest that observer bias affects data quality especially in unblinded studies (Holman *et al*, 2015). A recent meta-analysis showed that a lack of blindness was associated with an increase in effect size of approximately twenty-seven percent and suggested that this effect of blindness resulted from observer bias (Holman *et al*, 2015). The same researchers reported that blinded papers had a significantly lower proportion of significant results. In addition, given that the current data suggests that TC ratings may be unreliable and should not form part of the asymmetry scale, this calls into question Philippi and colleagues (2006a) dichotomisation of patients into 'normal' and 'asymmetric' groups for further analysis. In the current study, external observers were used to score the IPA measurements, therefore, avoiding observer bias and improving the reliability of the data. In addition, the current study had a larger sample size than the Philippi *et al* study and different methods were attempted to group participants. However, results were found to be unstable thus suggesting that Philippi *et al* (2006a) results could have been a false positive.

Behavioural subsets deemed to most clearly reflect the differences between infants with settled and unsettled behaviours (Putnam, 2013, personal communication) were also tested for effects. The analysis of 'Distress to Limitations' was of particular interest as this subset is believed to reflect the core of parental perceptions of difficult temperament (Bates and Bayles, 1984). It has been suggested that retrospective parent-reports of temperament after colic has resolved may be biased by the experience of living with an infant who had colic. As such, there are several reports of inconsistencies in correlations between observed and maternally rated infant behaviour (see Worobey, 2009). However, White *et al* (2000) reported good cross-situational stability between Rothbart's (1981) original IBQ subset 'Distress to Limitations' and laboratory observations of crying and consolability, when assessing parent perceptions of infant behaviour. The current study detected no significant differences between the specified IBQ-Rs subsets, including the 'Distress to Limitations' subset, and the CRD High/Low dichotomised groups. Therefore, a relationship between the IBQ-Rs subsets, which would be most associated with infant unsettledness and CRD was not detectible. These results suggest that there is no association between CRD and unsettled infant behaviour, as reported in the IBQ-Rs subsets, in twelve- to sixteen-week-old infants. The relationship between of CRD and other infant behaviour assessment tools is worth examining in future studies.

Post-hoc tests showed that for females, SUR scores were significantly higher for the low CRD group than for the high CRD group, indicating that female infants who score highly in the positive affectivity component of the IBQ-Rs are more likely to fall into the low CRD group. Positive Affectivity/Surgency (SUR) components include the subsets of approach, vocal reactivity, high intensity pleasure, smiling and laughter, activity level and perceptual sensitivity (Putnam *et al*, 2014). These are all behaviours associated with happy and excitable infants who like attention (Casalin *et al*, 2012). They are sociable, interacting with people and their surroundings but they do not like to be left unattended (Casalin *et al*, 2012). This finding is the first indication that there may be a relationship between low CRD and positive behavioural traits. Further testing of this finding is needed to examine if the relationship between the low CRD and high SUR scores in females is associated with a healthy musculoskeletal system, as the nature of the dichotomised data analyses was somewhat unstable. For males, there was no significant difference in SUR scores.

The NEG broad component comprised of negative emotionality behaviours such as sadness, distress to limitations and fear (Putnam *et al*, 2014). These babies tend to be demanding, fearful and anxious. They are easily startled and then difficult to settle (Casalin *et al*, 2012). They are clingy, not happy in unfamiliar company and can be difficult to get to sleep (Casalin *et al*, 2012). This category of infants are the ones that generally fall into the irritable, unsoothable and unsettled behaviours (DeSantis *et al,* 2011). Female infants were rated significantly higher on the NEG subscale than males, which replicates the finding of Putnam *et al* (2006) and may suggest that females are more likely to present with unsettled behaviour than males. Previous reports have also found a predominance of female infants with unsettled behaviour (Hill *et al,* 1992), although St James-Roberts & Halil (1991) reported no interaction between gender and perceived crying amounts. As there was no interaction of gender and CRD in the current study, this gender difference is not associated with the CRD score.

The REG broad component refers to the regulatory capacity of infants and includes the subsets duration of orienting, low intensity pleasure, cuddliness and soothability (Putnam *et al*, 2014). These babies are settled and undemanding, though they like to be held and cuddled (Casalin *et al*, 2012). They are less interactive and responsive than the SUR babies and soothe easily in most situations. REG babies have been shown to predict the adult personality trait of conscientiousness (Putnam *et al*, 2008). There were no effects of gender with REG behaviours, and no association with CRD.

The IBQ-Rs was chosen as it permitted the measurement of fine-grained subsets (e.g. multiple types of negative affectivity) to match narrow research questions with assessment of other broad factors to facilitate more exploratory analyses. However, claims of the reliability and validity of the IBQ-Rs measurement for three-month-old infants are challenged by the findings of the current study. In addition, Putnam *et al* (2014) assessments of external validity were carried out with short form scale scores that were extracted from revised version of the IBQ data (i.e. IBQ-R). The context of being in the full form of the IBQ-R makes the subset data from it a different questionnaire to the IBQ-Rs. Validity and reliability data cannot be generalised from a full questionnaire to a subset of the items extracted from that questionnaire. It is possible that different findings might be obtained if the short form itself were administered. Future studies investigating these forms of validity are necessary to test the convergence of these instruments with other assessment methods.

It was expected that some questions would not be relevant for young infants, therefore, in consultation with Putnam (personal communication, July 2013) a clarification was appended to the IBQ-Rs (Appendix 4). Response rates to the individual IBQ-Rs questions were good with ninety percent being scored on the numerical scale. Almost all (>99%) of the missing data were assigned 'does not apply', i.e. parents did respond to the item and it was therefore not technically missing data, rather than the response was not scorable. Although 'does not apply' responses cannot help us understand individual differences in infant temperament, they do provide information about how parents interact with the IBQ-Rs and indicate the difficulties parents have in rating their infant's behaviour at the age range used in the current study.

It was noted that twenty-three percent of the 'does not apply' responses were connected to four IBQ-Rs questions, which related to the accomplishment of activities and reactions to audible and visual stimuli unsuitable for young infants (e.g. looking at books, stacking blocks, noticing distant sounds and sights). This would indicate that these behaviours are not yet apparent in the repertoires of many three-month-old infants. The scoring of these individual questions would have an impact on the fourteen resulting IBQ-Rs subsets. In this study, the subsets most affected by 'does not apply' response rates were Perceptual Sensitivity (37%), Approach (25%), Duration of Orienting (16%) and High Intensity Pleasure (12%). In spite of the high rate of 'does not apply' responses, the overall response rates for all IBQ-Rs questions were high enough to use and the data was still valid for further analysis with CRD and patient demographics.

Recent research by Giesbrecht *et al* (2014) reported a similar pattern of 'does not apply' responses in the IBQ-Rs to those in the current study, although to a greater extent. They examined the number of 'does not apply' responses on the IBQ-Rs form for three- and six-month-old babies and found a problem at three months. Giesbrecht and colleagues (2014) found that the mean number of 'does not apply' items exceeded fifty percent in the Perceptual Sensitivity and Approach scales at three months. Duration of Orienting and High Intensity Pleasure had 'does not apply' responses exceeding thirty percent. Giesbrecht *et al* (2014) found that the difficulty with these scales appears to resolve by the time infants reach six-months of age, with the exception of the Perceptual Sensitivity scale.

Giesbrecht *et al* (2014) suggest the removal of subsets with 'does not apply' responses above thirty percent on the basis that differences in the observed reliability, means and longitudinal stability of temperament can be attributed to the presence of 'does not apply' responses, and interfere with assessment of infant temperament using the IBQ-Rs. In the current study 'does not apply' responses above thirty percent accounted for Perceptual Sensitivity only and removal of this subset made no significant difference to results. Although the findings in this study would suggest the effects of 'does not apply' may not be as problematic as Giesbrecht and colleagues (2014) propose, the consistency between the two studies would indicate that the IBQ-Rs may need to be revised, and then validated, for use with three-month-old infants. Putnam *et al* (2014) also suggest choosing parts of questionnaires, or the use of "hybrid" measures where appropriate, given the goals and hypotheses of a particular investigation. However, researchers with interests in discrete traits are advised to carefully consider the implications of abbreviation for individual scales when deciding on whether to use the IBQ forms (Putnam *et al*, 2014). Any change to a questionnaire nullifies all measures of validity and reliability as it becomes a new questionnaire (Juniper, 2009). Therefore validation studies are necessary every time a new combination of subsets are selected for a particular study.

Giesbrecht *et al* (2014) reported that both infant age and parity were associated with the prevalence of 'does not apply' responses. The narrow age range in the current study of twelve- to sixteen- weeks found no correlation with the 'does not apply' responses. Similarly, Gartstein and Rothbart (2003) did not find age-related changes in 'does not apply' responses when analysing their IBQ-R data using age brackets (e.g. 3–6 months, 6–9 months, 9–12 months), which may have obscured age-related differences. Giesbrecht *et al* (2014) made a clear distinction between the three- and six-month-old infants by excluding infants in the mid-age range and suggested that this enhanced the strong decrease in the number of 'does not apply' items from three- to six-months of age. Additional research is required to indicate whether the various scales of the standard and short form instruments are appropriate for very young infants. However, a better approach might be to develop *de novo* a short-form questionnaire for younger children based perhaps on behavioural observation of and qualitative interviews about young infant behaviour.

The possibility that the age range in this study of twelve- to sixteen- weeks was not optimal for investigating relationships with unsettled infant behaviour needs exploration, as the natural course of unsettled behaviour peaks around six-weeks-old and normally decreases by sixteen weeks (Barr *et al*, 1988, Barr *et al*, 1989; Brazelton, 1962; Hill *et al*, 1992; Hiscock & Jordan, 2004). This is of particular importance when the impact on family relations also peaks around the same time (Overpeck *et al*, 1998) and, while apparently innocuous, an infant's unsettled behaviour can prompt lasting parental distress (Forsyth *et al*, 1985; Miller *et al*, Rautava *et al*, 1995). To minimize parental biases associated with poor recall, in the IBQ-Rs parents are asked to report the frequency with which infants have enacted specific behaviours in common situations during the past week or two weeks (Putnam *et al*, 2014). Therefore, there is a risk that the application of the IBQ-Rs at twelve- to sixteen- weeks did not capture the true prevalence of unsettled behaviour in these infants and the results should be treated with caution. Targeting infants as young as six-weeks-old was considered for this study, given that the original IBQ (Rothbart, 1981) was used with infants from two-weeks-old (Worobey, 1986; Worobey & Blajda, 1989). However, Putnam *et al* (2014) demonstrated adequate internal consistency in the IBQ-Rs for twelve-week-old infants, thus deciding the minimum age range for this study. Although participant burden sometimes dictates that a shorter form of the scale must be used, this choice should be balanced with missing data considerations, especially in early infancy when the rate of 'does not apply' responses for the IBQ-Rs is relatively high.

Although the aim of this study to find a relationship between musculoskeletal dysfunction and unsettled infant behaviour remains unproven, there are several other researched theories about contributing factors to unsettled infant behaviour, which are examined in detail in chapters 2-6. These include gastrointestinal problems due to gastro-oesophageal reflux disease (GORD) (Douglas & Hiscock, 2010; Lim, 2006), cows' milk protein allergy (CMPA) (Forsyth, 1989), lactose intolerance (Miller *et al*, 1988; Moore *et al*, 1988), altered intestinal microbiota (Chau *et al*, 2015; de Weerth *et al*, 2013; Savino *et al*, 2010; Sung *et al*, 2014) and excess gas (Carey, 1984; Illingworth, 1985; Miller & Barr, 1991). In spite of the high prevalence of unsettled infant behaviour, remarkably few infants have been found to have organic disease (Gormally & Barr, 1997). For example, only one-sixth of infants with persistent crying have a diagnosis of pathological GORD (Heine *et al*, 2006) and there is no evidence for the use of anti-secretory drugs or prokinetic agents in infants with physiologic regurgitation (Heine *et al*, 2006; Vandenplas *et al*, 2013), especially if associated with over-feeding (Khoshoo *et al*, 2000). Parental education regarding conservative management strategies, which include elevation, positioning and feeding techniques, should be considered (Armstrong *et al*, 2000) and any unnecessary risks of adverse outcomes of pharmaceutical interventions avoided (Augood *et al*, 2003) (Vanderplas *et al*, 2009).

CMPA has been associated with unsettled infant behaviour (Barr, 1996; Gormally & Barr, 1997; Hill *et al*, 2005; Lucassan *et al*, 1998; Miller & Barr, 1991; Treem,

1994) and, in fact, there is a suggested relationship between GORD and CMPA (Vanderplas *et al*, 2007). However, crying alone is not regarded a sufficient diagnostic sign of a food allergy or intolerance (Liebman, 1981) and a CMP free diet is recommended only when a complete remission of symptoms is achieved. It has also been hypothesised that some babies have a transient underlying lactase deficiency, leading to a build-up of lactose derived from breast milk or infant formula but its role remains uncertain (Hiscock & Jordan, 2004). The use of lactose-free formula or lactase drops in breastfed infants has variable results (Hiscock & Jordan, 2004; Hyams *et al,* 1989; Miller *et al*, 1990; Moore *et al*, 1988). Unsettled infant behaviour has been associated with a lack of microbial diversity of the intestinal microbiota in the early days of life (de Weerth *et al*, 2013) and, perhaps the most promising research in recent times are the benefits reported for probiotic usage, particularly Lactobacillus reuteri DSM 17938 (Chau *et al*, 2015; Savino *et al*, 2010; Szajewska *et al*, 2013). However, data in this area is preliminary and more research is required to develop tests that are suitable for routine diagnostic screening.

A relationship between regulatory problems and both infantile colic (White *et al,* 2000) and infant temperament (Buss & Plomin, 1984; Rothbart, 1986) has been suggested as well as transient developmental dysregulation of the nervous system (Brazelton, 1990). In addition, less than optimal parent-infant interactions have been implicated in unsettled infant behaviour (Carey, 1984; Goldfeld *et al*, 2003; Wolke *et al*, 1994). Keefe *et al* (2006) suggested that disruptions or inconsistencies in parenting or the surrounding environment overstimulate the infant, resulting in crying that the infant does not yet have the maturity to regulate. Problems with self-regulation, including sleep, feeding, state control, self-calming, sensory reactivity, mood regulation, and emotional and behavioural control, have been documented during infancy (DeGangi *et al*, 2000). The relationship between infantile colic and maternal depression has been found in many cross-sectional studies (Akman *et al*, 2006; Armstrong *et al*, 1998; Armstrong *et al*, 2000; Barnett *et al*, 1993; Carey, 1968; Howell *et al*, 2006; McMahon *et al*, 2001; Milgrom *et al*, 1995; Miller *et al*, 1993; Miller-Loncar *et al*, 2004; Murray, 1997; Papousek & Papousek, 1990;

Papousek & von Hofacker, 1998; Pauli-Pott *et al*, 2000; Wake *et al*, 2006) indicating the importance of the mother-child dyad. Yet the causal direction of these associations remains uncertain (Armstrong *et al*, 1998; Mc Callum *et al*, 2011; Miller *et al*, 1993).

The complexities of examining unsettled infant behaviour are apparent in the continued lack of understanding about what constitutes unsettled 'colicky' behaviour and normal developmental crying behaviours. Differentiating between these two phenomena is important, so that future research into all the theories associated with unsettled behaviour can be compared and cross-referenced, and appropriate measures can be taken in managing these infants and supporting their families. This would require universal usage of defined terminology, multidisciplinary communication, appropriate referral and early intervention.

It could also be that the underlying model of disease-dysfunction is wrong or that the explanations and theory put forward by osteopathic theorists are wrong even though the practice can be demonstrated to be beneficial or at least perceived to be beneficial by patients. As we are dealing with subtle, complex multifactorial situations which are accentuated in infants because they are also at immature stages of development, the conventional linear cause-effect models may not apply at all. Although we are still a very long way from knowing what an alternative better explanation might be, acknowledging and exploring the biopsychosocial factors which operate in an osteopathic consultation and how this effects the overall outcome, is vital to understanding of how unsettled infants and their familes can be supported into the future. Reliance on self-reported and self-analysed accounts of osteopathic treatment is no longer sufficient, we need to spend more time analysing exactly what it is that effective osteopaths do.

13.2 Strengths and limitations

The findings of this study may have been limited by a form of spectrum bias, i.e. bias which exists when the population under investigation does not reflect the general population or the clinically relevant population (Mower, 1999). To avoid confounding effects from other interventions, infants who had been referred to or treated with manual therapy, including osteopathy and physiotherapy, were excluded from this study. This is of particular significance in the local population where the study was conducted. The osteopathy clinic is a frequent route of referral from other health care professionals for infants with unsettled behaviour. During the data collection period from November 2013 to January 2015, 203 infants under sixteen-weeks-old attended the osteopathy clinic with symptoms of unsettled behaviour. The birth rate in the community for the same period was 1793 live births. Therefore, eleven percent of the children born in the local area attended the osteopathy clinic with unsettled behaviour and would have been excluded from the study. As unsettled behaviour affects up to twenty-five percent of infants (de Weerth *et al*, 2013), it can be estimated from these figures that a significant proportion of infants with unsettled behaviour would have been excluded from the study. Thus potential recruits were likely to be unrepresentative of patients in the local community and the study may be biased towards a more settled infant population. Participants were then further selected according to trial eligibility criteria, as a proportion of participants were excluded due to non-compliance and distress during the video-recording part of the study. This may have resulted in more 'settled' babies being recruited from the PHC's and is potentially another form of spectrum bias. Spectrum bias may account for differences in reported results between investigations (Mower, 1999).

The field of unsettled infant behaviour is complex with multiple interrelated factors, assessment of which might have informed a more comprehensive approach to results interpretation. Some salient factors of mother and infant, which have previously been associated with infant behaviour and/or asymmetrical postures, were not assessed in this study. Although previous associations have been made between infant behaviour and pregnancy health (Hawthorn, 2004), birth history (Hiscock & Jordan, 2004; Vejsgaard Vestager *et al*, 2007; Wilberg & Nilsson, 2000) and interventions used (Thomas, 1981), feeding modality (Cohen Engler *et al*, 2012), maternal age and health both physical and mental (Hogdall *et al*, 1991; Rautava *et al*, 1993), these were not measured. Similarly, details of in-utero foetal position, previously associated with asymmetry (Cheng & Au, 1994, Deidrich *et al*, 2002; Lloyd-Roberts & Pilcher, 1965; Rosegger & Steinwendner, 1992; Wynne-Davies, 1975), may have elicited significant findings. However, the current study was designed to identify if the IPA scale could be used as a measure of musculoskeletal dysfunction and then find a relationship with infant behaviour. Additional information requirements were limited because the ninety-one item IBQ-Rs would take thirty minutes to complete (Putnam *et al*, 2014), already placing significant time demands on parents. Birth order, birth weight, weight gain and sex were measured, as previous associations have been made with both unsettled behaviour and infant asymmetry (Putnam *et al*, 2006; Shamji *et al*, 2012; Søndergaard *et al*, 2000). As the research took place following the infants' public health check, these details were readily available. Parental demographic data was not collected, although this has previously been found to impact on infant behaviour (Armstrong *et al*, 2000; Barr, 1998b; Canivet *et al*, 2005; Rautava *et al*, 1993; Reijneveld *et al*, 2001). Studies have found that successful recruitment can be as low as twenty-five percent and parental participants are often mature, well educated, and in a stable relationship (Barr *et al*, 1988; Hunziker & Barr, 1986; St James-Roberts *et al*, 1995) which may bias results.

The sample size achievable when studying infants is limited by a number of factors. Due to the sensitive nature of research with infants, particularly when video-recording undressed infants, ethical considerations were rigorous. Recruitment in this study was permitted only through PHC's. Three clinics were selected, which considered the socio-economic representative of patients in the local community (Rothwell, 2005) but allowed access to a small proportion of these babies which restricted the sample size. In addition, parents are naturally protective about their babies and need a lot of reassurance about any interference they see as unnecessary.

The information pack in this study was designed to reassure parents with detailed information, as previous studies on infant temperament have shown this to play an important role in participant recruitment (Nader, 1985).

The relative short recruitment period of twelve- to sixteen- weeks limited the window of opportunity to capture recruits. Attendance at PHC's can be unreliable for a variety of reasons, including infant sickness, and infants can easily fall outside the study target age. The rapid musculoskeletal development in the period up to sixteen weeks (Cioni *et al*, 2000), and the interaction of this and behaviour, is likely to be more complex than initially appreciated. Targeting a narrow age range only provides a 'snap shot' of interactions at this point in time. Boere-Boonekamp and van der Linden-Kuiper (2001) noted a sharp reduction in the prevalence of positional preference from eleven percent at sixteen-weeks of age to three percent by twenty-three-weeks of age. Equally, as the peak time for unsettled behaviour is reported by many researchers to be six-weeks old (e.g. Brazelton, 1962) and the IBQ-Rs fails to capture infants during this period, one additional question which may have enhanced interpretation of the data would have been 'Has your baby ever suffered with unsettled behaviour (i.e. crying for more than three hours a day for more than three days in the week)?' This could be used to investigate if there were a proportion of babies who had been previously unsettled but were missed due to the timing of the study.

There were several strengths associated with the current study. Understanding infant behaviour is limited in part by ethical issues which restrict unnecessary invasive investigations in children (Fitzgerald & Walker, 2009). Therefore, research studies frequently struggle to recruit adequate sample sizes to conduct acceptable statistics. The current study recruited a sample size of fifty-eight participants, a larger sample than any of the Philippi *et al* studies (2004, 2006a, 2006b). As the participants were referred through three PHC's based on age of baby and consent of parents, bias in the selection of recruits was avoided. The results of this study are more likely to demonstrate external validity than the previous studies by Philippi and colleagues, as the video-scoring was conducted by five independent osteopaths in their clinical settings.

Parental recall of data in the IBQ-Rs would have good expected accuracy, with limited perception bias, as it was requested from the previous one week or two weeks rather than over several months, which can be unreliable (see Wurmser *et al*, 2001). The potential to have several independent observers analyse the same video-recordings allows for repeat checking of unclear IPA readings and increases the validity of the test results. Finally, the application for ethical approval to allow research into the collection of sensitive data necessitated much consideration into participant recruitment and study design. The process of exploring ethically acceptable approaches to data collection without compromising the integrity of the design resulted in a greater appreciation for the sensitivities in paediatric research.

13.3 Implications and recommendations

Although the current study showed no association between musculoskeletal dysfunction and unsettled infant behaviour the possibility remains that the IPA and IBQ-Rs measures were unable to detect an association, rather than one does not exist. To fully assess the utility of the IPA measurement scale, a diagnostic accuracy study should be conducted in which asymmetrical parameters are measured for infants already requiring radiographs. Such a study could test the proposal by Philippi *et al* (2004) that the IPA scale could provide a non-invasive alternative to radiograph. However, such studies should be considered with caution given that the current study provides no evidence that an association exists.

Recognising the need to inform parents on expected infant behaviours and provide advice on optimal infant handling and positioning techniques is required across all healthcare providers involved in the management of unsettled infant behaviour. A principal issue is a lack of clearly defined terminology and categories for unsettled behaviour. The development of osteopathic training to establish consistent terminology and categorisations of infant behaviour that can be used within and outside of the profession could enhance the management of these infants, so that a cooperative multidisciplinary approach can be pursued. Defining characteristics, if not exact aetiology, would be a first step toward subgrouping infants afflicted with the condition and a starting point for this might be within osteopathy.

This study highlights the importance of choosing a suitable data collection approach. Parent-report questionnaires have distinct advantages but are challenged in the research of very young infants. Giesbrecht *et al* (2014) suggest delaying assessments until infants are at least six months of age. However, assessing infant temperament earlier than six-months-old has become an important area of research and the recommendation to wait prohibits further research into early infant behaviour, which is unsatisfactory (Giesbrecht *et al*, 2014). For researchers interested in the behaviour patterns of very young children, this study should encourage further investigation and development of specific age appropriate measurement tools.

The use of an IPA-type measurement scale in research, and potentially clinical practice, needs further examination. The practicalities of a user-friendly and standardised measurement scale, which avoids exposure to harmful radiation, remains desirable in assessing the asymmetric presentation of infants. Previous validation of the four IPA parameters (Philippi 2004, 2006a, 2006b) was not supported in the current study but the use of CRD measurement requires more rigorous testing. The unreliable findings of TC in the current study should be re-evaluated following more extensive training sessions however being cognisant that extra training demands may reduce its utility as a clinical tool.

Osteopathic practice needs to examine what component of infant care relies solely on musculoskeletal treatment and if confirmation bias plays a role, i.e. the possibility of looking for musculoskeletal dysfunctions leads to finding them. Confirmation biases can prevent us from considering important information when making decisions. Composite outcomes sometimes combine events of very different severity, and treatment effects can be driven by the least important outcome (Rothwell, 2005). For example, it is possible that providing parents with advice on normal developmental behaviours and positioning advice has greater benefit than the osteopathic treatment. The importance of patient preference for treatment type (e.g. natural approach versus medication), placebo effects, and the practitioner-patient relationship should not be underestimated. Training of osteopaths should also include the skills of identifying potential positioning and handling problems and alerting parents to alternative approaches as part of the musculoskeletal assessment of the infant. For those already trained, accessible postgraduate training specific to new knowledge in the field of paediatric osteopathy, needs to be developed. Constructing a case history to include more detailed information on holding, soothing, feeding and sleeping positions could prove valuable so more comprehensive management strategies can be delivered. A better understanding of the role for osteopaths in paediatric care is required, which is consistent with the holistic approach of osteopathy, to examine how this can enrich parental confidence and impact on the infant behaviour.

13.4 Future studies

Research in this young age group is problematic for several reasons. Rapid changes in development take place over short time spans (Cioni *et al,* 2000) which can make results of research unstable. Determining whether the instability is associated with the research methodologies or the study sample can be challenging. Validation of a standardised asymmetry model opens the opportunity for comparative studies of other therapeutic concepts. Further research is necessary to investigate whether a reliable measure of asymmetry can be developed, by examining combinations of individual movement patterns. This could then be tested for its utility in a clinical setting to detect and manage infantile asymmetry, and future studies in infant behaviour.

Consistent terminology and crying categorisation is essential to inform future research in early identification and treatment of unsettled infant behaviour. Developing a cross-sectional study to investigate the language used by parents and practitioners to describe unsettled infant behaviour would be an important advancement in this field. Equally, a qualitative study to investigate, in depth, what health-care professionals understand by terms such as ‘unsettled infant behaviour’, ‘colic’, ‘problematic crying’, ‘difficult temperament’, etc., would enhance cross-professional communication. The ability to define infant behaviours in terms of other parameters instead of crying time helps to alleviate one of the main controversies, namely that the crying time in research trials may be too close to the referenced norm to have significant research or clinical utility (Miller, 2014). In addition, the ability to distinguish between normal developmental behaviour patterns and unsettled infant behaviour may go some way to develop and improve pathways for inclusion and exclusion criteria for research studies, to more closely identify the characteristics of the infants under study. Due to the possibility of spectrum bias in the current study, it would be useful in future work to apply behaviour analysis and asymmetry scales to the infants referred to the clinic with unsettled behaviour and compare this with the results of normal babies in the community.

The IPA video-recordings could be re-examined, by consent, to investigate detection levels of early signs of asymmetry among healthcare professionals by showing the same video-clip of baby movements to multiple healthcare professionals. Analysis of intra-observer reliability across different practitioners could help identify those best suited to making accurate diagnoses. In addition, the video-recordings could be re-examined for evidence of asymmetric features including plagiocephaly, oblique body position and asymmetric foot position as suggested by Philippi *et al* (2006b), to investigate possible associations with recorded CRD measurements. The store of video recordings allows for follow-up studies into responses to different treatment protocols. The long-term sequelaes of undetected or untreated asymmetry could also be analysed retrospectively from the video-recordings.

A retrospective study of inter-uterine position and birth history could be collected from medical records of the current study group and possible effects with IBQ-Rs subsets explored. This could enhance the knowledge base on the effects of pre-, peri- and post-natal history of infant behaviour. This would allow further examination of associations with asymmetrical findings on the video-recordings.

Van Vlimmeren *et al* (2004) suggest that studies on asymmetry in infancy should start with phenotypical analysis searching for secondary effects (e.g. muscular functional imbalance and abnormal head position) and lead to primary causes (e.g. intrauterine crowding and trauma induced haemorrhage).

Investigating the effects of cultural differences in parenting styles and how this impacts on infant behaviour would be useful and could also be attempted retrospectively from the medical records. There would be limitations in the current study as the sample size and community is not large enough to collect adequate data. Cultural differences in infant management and effects on infant behaviour have been identified (St James-Roberts *et al*, 2006). Any future study on infant behaviour should endeavour to include these details at the data collection stage so that pertinent interactions can be identified and better understood.

The positive impact of supportive information, advice and care in the transition to parenthood, along with a multidisciplinary approach to managing unsettled infant behaviour is evident throughout the literature (e.g. Douglas *et al*, 2012). It is reported that addressing infant positioning plays an important role in the management of some asymmetrical conditions such as deformational plagiocephaly, positional preference, torticollis and scoliosis (Cavalier *et al*, 2011; Saeed *et al*, 2008; van Vlimmeren *et al*, 2008). It can be assumed, therefore, that by altering infant position, the corrective action on the asymmetric condition may be associated with effects to the musculoskeletal system. Osteopathic practitioners' work focuses on the correct functioning of the musculoskeletal system (Turi *et al*, 2013) and the skills of the osteopath in providing optimal infant handling and positioning advice should not be underestimated. Possible future work should assess how the effects of OMT on asymmetry compare with the effects of handling and positioning advice.

Education on infant positioning and handling also has shown benefits for some conditions associated with unsettled infant behaviour (e.g. reflux) (Vandenplas *et al*, 2013). An alternative approach could be to assess the effects of osteopathy on unsettled infant behaviour compared to a structured information, support and advice strategy. These studies could highlight aspects of paediatric treatment that are most effective for managing behaviour disturbance. This would help to establish appropriate advice and counselling to parents of unsettled infants, and as a cost-benefit analysis of the treatments used in our society (Olafsdottir, 1999).

Methodological shortcomings in the research of unsettled behaviour, including inconsistent definitions and inadequate study designs, have restricted the confidence that can be placed in the findings of many works and consequently, evidence is contradictory. This uncertainty, along with the frequent occurrence of unsettled behaviour, the potential impact on the family, and the absence of an effective cure (Garrison & Christakis, 2000) underlines the importance of continued research. Existing research does not allow the non-specific effects related to the delivery of the intervention to be separated from any specific effects of the interventions. Thus, any positive outcomes may include both specific and non-specific effects (Underwood, 2009). The entire approach to infant management from an osteopathic perspective needs further exploration to test the efficacy of osteopathic treatments for unsettled behaviour. Such studies should be sham controlled to match for those aspects of osteopathic interventions other than the musculoskeletal treatment. This would provide a strong test of anecdotal claims that osteopathic treatment release stresses and strains that cause infant unsettledness.

Chapter 14 - Conclusion

Unsettled infant behaviour is recognised as a significant problem particularly in the first twelve weeks of a baby's life (Wake *et al*, 2006). Although osteopaths treat infants with unsettled behaviour, a causal relationship between the musculoskeletal system and infant behaviour is unproven and evidence for the benefits of osteopathic treatment is anecdotal (Lim, 2006). Examining musculoskeletal discomfort in infants is challenged by the inability of infants to articulate clear reactions to the usual musculoskeletal testing applied to adults (Finley *et al*, 2005). Any improvement in unsettled symptoms cannot be attributed to osteopathic treatment without consideration of the non-specific effects of reassurance, attention and support (Lim, 2006), as well as the phenomenon of regression to the mean (Senn, 2011) and placebo effects.

The IPA scale measured asymmetry in infants, which can be a sign of musculoskeletal dysfunction, in an easy-to-use and non-invasive way (Philippi *et al*, 2004). This presented an opportunity to examine a musculoskeletal relationship with unsettled infant behaviour. Improvements demonstrated in IPA following osteopathic treatment indicated a role for osteopathy in the treatment of babies (Philippi *et al*, 2006a). The overall purpose of this study was to address a paucity of research into the appropriateness of osteopathic treatment for unsettled infant behaviour, by investigating the relationship between infant behaviour and musculoskeletal health. What instigated this study were significant gaps found in the research.

The results of this study do not suggest a relationship between musculoskeletal dysfunction using the IPA measurement scale and unsettled infant behaviour using the IBQ-Rs in twelve- to sixteen- week old infants. A significant difference between high and low CRD groups for Surgency was detected in female babies. It is not clear whether this effect is suggestive of a relationship or if a different approach would draw out the data more accurately, but conclusions cannot be drawn without further examination. What can be concluded is that the IPA measurement scale, in its current format, does not appear to be a good method of assessing musculoskeletal dysfunction in infants.

This study also identified stability issues in the IBQ-Rs for twelve- to sixteen-week-old infants and future work requires the validation of a reliable infant behaviour assessment tool for twelve-week-old infants. This study indicates that the relationship between unsettled infant behaviour and musculoskeletal dysfunction may be more complex than originally appreciated or that different tools are required for assessing musculoskeletal tension and infant behaviour for babies aged twelve to sixteen weeks.

The high prevalence of unsettled behaviour in infants, the large number of children referred for additional diagnostic evaluation and/or treatment (McCallum *et al*, 2011), and the resulting high medical expenses (Morris *et al*, 2001) strongly call for a primary preventative approach. There is a requirement to provide information, support and advice during the transition to motherhood in order to clarify normal crying behaviours and give confidence in parenting techniques (Douglas *et al*, 2012). Intervention into the management of infants needs to be early and engage a multidisciplinary approach (Douglas *et al*, 2012; Martin & Kasperski, 2010). This can only be achieved by establishing common terminology and infant behaviour categorisation for all paediatric healthcare practitioners to facilitate communication across professions. There may be a role within osteopathy to embrace the development of such language classifications, to incorporate this into under- and post-graduate training programmes and to disseminate it across paediatric professions. There is also a responsibility within osteopathy to examine in more detail how the influence of positioning and handling practices on correcting asymmetry conditions in infancy relates to the musculoskeletal system, and perhaps other paediatric conditions such as unsettled infant behaviour. A causal relationship between unsettled infant behaviour and musculoskeletal dysfunction is still unproven and the role of osteopathy in treating the musculoskeletal system for unsettled infant behaviour remains unsupported.

Chapter 15 – List of References

Aarnivala, H., Vuollo, V., Harila, V., Heikkinen, T., Pirttiniemi, P. & Valkama, A. (2015) Preventing deformational plagiocephaly through parent guidance: a randomized, controlled trial. *European Journal of Pediatrics* 174(9):1197-1208.

Adams, SM.; Jones, DR., Esmail, A. & Mitchell, EA. (2004) What affects the age of first sleeping through the night? *Journal of Paediatrics and Child Health* 40:96–101.

Agran, PF., Anderson, C., Winn, D., Trent, R., Walton-Haynes, L. & Thayer, S. (2003) Rates of pediatric injuries by 3-month intervals for children 0 to 3 years of age. *Pediatrics* 111:e683–e692.

Agresti, A. (1990) *Categorical data analysis*. New York: John Wiley and Sons.

Akman, I., Kuscu, K., Ozdemir, N., Yurdakul, Z., Solakoglu, M. & Orhan, L. (2006) Mothers' postpartum psychological adjustment and infantile colic. *Archives of Disease in Childhood* 91:417–419.

Alcantara, J. & Anderson, R. (2008) Chiropractic care of a pediatric patient with symptoms associated with gastroesophageal reflux disease, fuss-cry-irritability with sleep disorder syndrome and irritable infant syndrome of musculoskeletal origin *The Journal of the Canadian Chiropractic Association* 52(4):248—255.

Alcantara, J. & Mayer, DM. (2008) The successful chiropractic care of pediatric patients with chronic constipation: A case series and selective review of the literature. *Clinical Chiropractic* 11:138—147.

Alderberth, I. & Wold, AE. (2009) Establishment of the gut microbiota in Western infants. *Acta Paediatrica* 98:229-238.

Allen, DM. (2005) Observations from Normal Newborn Osteopathic Evaluations in Frymann, VM. *Proceedings of the International Research Conference, Celebrating the 20th Anniversary of the Osteopathic Centre for Children*. AAO Indianapolis.

Alvarez M. (2004) Caregiving and early infant crying in a Danish community. *Journal of Developmental and Behavioral Pediatrics* 2:91–98.

American Academy of Pediatrics, Committee on Nutrition. (2000) Hypoallergenic infant formulas. *Pediatrics* 106:346-349.

Amiel-Tison, C. & Soyez-Papiernik, E. (2009) The role of osteopathy in the correction of skull deformations in newborns and infants. *Osteopathic Medicine, Journal of holistic therapies* 10(4):10-15.

Anders, TF., Halpern, LF. & Hua, J. (1992) Sleeping through the night: a developmental perspective. *Pediatrics* 90:554–560.

Andersson, GB., Lucente, T., Davis, AM., Kappler, RE., Lipton, JA. & Leurgans, S. (1999) A comparison of osteopathic spinal manipulation with standard care for patients with low back pain. *New England Journal of Medicine* 341:1426–1431.

Arbuckle, BE. (1971) *The selected writings of Beryl E. Arbuckle, D.O., F.A.C.O.P*. Newark, OH: American Academy of Osteopathy; p.188.

Argenta, LC., Davis, LR., Wilson, JA. & Bell, WO. (1996) An increase in infant cranial deformity with supine sleeping position. *Journal of Craniofacial Surgery* 7:5-11.

Armstrong, KL., Quinn, RA. & Dadds, MR. (1994) The sleep patterns of normal children. *Medical Journal of Australia* 161: 202–206.

Armstrong, KL., O'Donnell, H., McCallum, R. & Dadds, M. (1998a) Childhood sleep problems: association with prenatal factors and maternal distress/depression. *Journal of Paediatrics and Child Health* 34: 263–6.

Armstrong, KL., Previtera, N. & McCallum, RN. (2000) Medicalizing normality? Management of irritability in babies. *Journal of Paediatrics and Child Health*. 36:301–305.

Armstrong, KL., Van Haeringen, AR., Dadds, MR. & Cash, R. (1998b) Sleep deprivation or postnatal depression in later infancy: separating the chicken from the egg. *Journal of Paediatrics and Child Health* 34:260-262.

Augood, C., MacLennan, S., Gilbert, R. & Logan, S. (2003) Cisapride treatment for gastro-oesophageal reflux in children. Cochrane Database System Review.

Balan, P., Kushnerenko, E., Sahlin, P., Huotilainen, M., Näätänen, R. & Hukki, J. (2002) Auditory ERPs reveal brain dysfunction in infants with plagiocephaly. *Journal of Craniofacial Surgery* 13:520–525.

Balon, AJ. (1997) Management of infantile colic. *American Family Physician* 55:235-242.

Bandyopadhyay, M., Small, R. & Watson, LF. (2010) Life with a new baby: how do immigrant and Australian-born women's experiences compare? *Australia and New Zealand Journal of Public Health* 34:412-421.

Barke, L., Gelman, S., Lipton, JA. (1997) A successful use of cranialsacral osteopathy in the treatment of post-traumatic headache following subarachnoid hemorrhage. *American Academy of Osteopathy Journal* 7(2):22-23.

Barnett, B., Lockhart, K., Bernard, D., Manicavasagar, V. & Dudley, M. (1993) Mood disorders among mothers of infants admitted to a mothercraft hospital. *Journal of Paediatrics and Child Health* 29:270–275.

Barr, RG. (1990a) The early crying paradox: a modest proposal. *Human Nature*. 1: 355-389.

Barr, RG. (1990b) The normal crying curve: what do we really know? *Developmental Medicine and Child Neurology* 32:356–362.

Barr, RG. (1991) Colic and gas. In: W.A. Walker, P.R. Durie and J.R. Hamilton (Eds.) *Pediatric gastrointestinal disease: pathophysiology, diagnosis and management*. Philadelphia: Decker (pp.55-61).

Barr, RG. (1995) Infant crying and colic: it's a family affair: invited commentary. *Infant Mental Health Journal* 16(3):218-220.

Barr, RG. (1996). Colic. In W. A. Walker, P. R. Durie, J. R. Hamilton, J. A. Walker-Smith, & J. B. Watkins (Eds.), *Pediatric gastrointestinal disease: Pathophysiology, diagnosis, and management* (2nd ed.). St. Louis, MO: Mosby (pp.241-250).

Barr, RG. (1997) Excessive crying. In M. Lewis & A. J. Sameroff (Eds.), *Handbook of developmental psychopathology* (2nd ed.) New York: Plenum Press.

Barr, RG. (1998a) Crying in the first year of life: good news in the midst of distress. *Child: Care, Health and Development*. 24(5):425-439.

Barr, RG (1998b) Colic and crying syndromes in infants. *Pediatrics* 102:1282-1286.

Barr, RG. (2000). Excessive crying. In M. Lewis & A.J. Sameroff (Eds.) *Handbook of Developmental Psychopathology* (2nd ed.). New York: Plenum Press.

Barr, RG., St. James-Roberts, I. & Keefe, MR. (2001) *New Evidence on Unexplained Early Infant Crying: Its Origins, Nature and Management.* Johnson & Johnson Pediatric Institute, L.L.C. Summary of a pediatric conference held in January 2000.

Barr, RG., Konner M., Bakeman R. & Adamson, L. (1991a) Crying in Kung San infants: a test of the cultural specificity hypothesis. *Developmental Medicine and Child Neurology* 33:601-610.

Barr, RG. & Geertsma, MA. (1993). Colic: The pain perplex. In N. L. Schechter, C. B. Berde, & M. Yaster (Eds.), *Pain in infants, children, and adolescents.* Philadelphia: Williams and Wilkins (pp.587-596).

Barr, RG., Hanley, J., Patterson, D. & Kingsnorth, WJ. (1984) Breath hydrogen excretion in normal newborn infants in repose to usual feeding patterns: Evidence for 'functional lactase insufficiency' beyond the first month of life. *Journal of Pediatrics* 104:527-533.

Barr, RG., Kramer, MS., Boisjoly, C., McVey-White, L. & Pless, IB. (1988) Parental diary of infant cry and fuss behaviour. *Archives of Disease in Childhood*. 63:380-387.

Barr, RG., Kramer, MS., Pless, IB., Boisjoly, C. & Leduc, D. (1989) Feeding and temperament as determinants of early infant crying/fussing behaviour. *Pediatrics*. 84: 524-521.

Barr, RG., McMullen, SJ., Spiess, H., Leduc, DG., Yaremko, J., Barfield, R., Francoeur, TE. & Hunziker UA. (1991b) Carrying as colic “therapy”: a randomized controlled trial. *Pediatrics* 87:623–630.

Barr, RG., Rotmans, A., Yaremko, J., Leduc, D. & Francoer, TE. (1992) The crying of infants with colic: A controlled empirical description. *Pediatrics* 90:14–21.

Bates, JE. (1983) Issues in the assessment of difficult temperament: A reply to Thomas, Chess, & Korn. *Merrill-Palmer Quarterly* 29:89–97.

Bates, JE. & Bayles, K. (1984) Objective and subjective components in mothers' perceptions of their children from age 6 month to 3 years. *Merrill-Palmer Quarterly* 30(2)111-130.

Belsky, J., Fish, M. & Isabella, R. (1991). Continuity and discontinuity in infant negative and positive emotionality: Family antecedents and attachment consequences. *Developmental Psychology* 27:421–431.

Berseth, CL., Johnston, WH., Stolz, SI., Harris, CL. & Mitmesser, SH. (2009) Clinical response to 2 commonly used switch formulas occurs within 1 day. *Clinical Pediatrics* 48:58–65.

Bialocerkowski, AE., Vladusic, SL. & Howell, SM. (2005) Conservative interventions for positional plagiocephaly: a systematic review. *Developmental medicine and child neurology* 47:563-570.

Biedermann, H. (2005) Manual therapy in children: proposals for an etiologic model. *Journal of Manipulative & Physiological Therapeutics* 28 (3):e1–e15.

Biedermann H. (2006) Manual Medicine of Functional Disorders in Children. *Medical Veritas* 3:803-814.

Biggs, WS. (2003) Diagnosis and management of positional head deformity. *American Family Physician* 67(9):1953-1956.

Binder, H., Eng, GD., Gaiser, JF. & Koch, B. (1987) Congenital muscular torticollis: results of conservative management with long-term follow-up in 85 cases. *Archives of Physical Medicine and Rehabilitation* 68:222-225.

Boere-Boonekamp, M. & van der Linden-Kuiper, L. (2001) Positional preference: prevalence in infants and follow-up after two years. *Pediatrics* 107(2):339-343.

Bohlin, G., Haughran, B. & Lindhagen, K. (1981) Dimensions of infant behavior. *Infant Behavior and Development* 4:83-96.

Boulton, TJC. & Rowley, MP. (1979) Nutritional studies during early childhood incidental III. Observations of temperament, habits, and experiences of iII-health *Australian Paediatric Journal* 15:87-90.

Bowlby, J. (1982). *Attachment* (2nd ed.). NewYork: Basic Books.

Brazelton, TB. (1962) Crying in infancy. *Pediatrics* 29:579-588.

Brazelton, TB. (1973) *Neonatal Behavioral Assessment Scale*. Philadephia: J.B. Lippincott.

Brazelton, TB. (1990) Crying and colic. *Infant Mental Health Journal* 11:349-356.

Brett, EM. (1991) *Paediatric Neurology.* New York: Churchill Livingstone.

Bridges, SJ., Chambers, TL. & Pople, IK. (2002) Plagiocephaly and head binding. *Archives of Disease in Childhood* 86:144–145.

Bridges, LJ., Palmer, SA., Morales, M., Hurtado, M., & Tsai, D. (1993). Agreement between affectively based observational and parent-report measures of temperament at infant age 6 months. *Infant Behavior and Development* 16:501–506.

Brough, N., Lindenmeyer, A., Thistlethwaite, J., Lewith, G. & Stewart-Brown, S. (2014) Perspectives on the effects and mechanisms of craniosacral therapy: A qualitative study of users' views. *European Journal of Integrative Medicine* 1-12.

Browning, M. & Miller, J. (2008) Comparison of the short-term effects of chiropractic spinal manipulation and occipito-sacral decompression in the treatment of infant colic: A single-blinded, randomised, comparison trial *Clinical Chiropractic* 11:122-129.

Brunetaeu, RJ. & Mulliken, JB. (1992) Frontal plagiocephaly: synostotic, compensational, or deformational. *Plastic and Reconstructive Surgery* 89:21-32.

Bruning, S. & Mc Mahon, C. (2009) The impact of infant crying on young women: A randomized controlled study *Journal of Reproductive and Infant Psychology* 7(2):206-220.

Budreau, G. (1987) Postnatal cranial molding and infant attractiveness: Implications for nursing. *Neonatal Network* 4:13-19.

Burton, K., McClune, TD., Clarke, RD. & Main, CJ. (2004) Long-term follow-up of patientswith low back pain attending for manipulative care: outcomes and predictors. *Manual Therapy* 9:30-35.

Buss, A. H., & Plomin, R. (1975). *A temperament theory of personality development*. New York: Wiley.

Buss, A. H., & Plomin, R. (1984). *Temperament: Early developing personality traits*. Hillsdale, New Jersey: Erlbaum.

Campbell, JRM. (1989) Dietary treatment of infant colic: a double-blind study. *Journal of the Royal College of General Practitioners* 39:11-14.

Canale, ST., Griffin, DW. & Hubbard, CN. (1982) Congenital muscular torticollis. A long-term follow-up. *The Journal of Bone and Joint Surgery (Am)* 64: 810-816.

Canivet, C., Hagander, B., Jakobsson, I. & Lanke, J. (1996) Infantile colic – less common than previously estimated? *Acta Paediatrica* 85:454-458.

Canivet, C., Jakobsson, I. & Hagander, B. (2000) Infantile colic: follow-up at four years of age: still more "emotional." *Acta Paediatrica* 89:13-17.

Canivet, CA., Stergren, PO., Rose, A. Jakobsson, IL. & Hagander, BM. (2005) Infantile colic and the role of trait anxiety during pregnancy in relation to psychosocial and socioeconomic factors. *Scandinavian Journal of Public Health* 33:26–34

Captier, G., Leboucq, N., Bigorre, M., Canovas, F., Bonnel, F., Bonnafe, A. & Montoya, P. (2003) Plagiocephaly: morphometry of the skull base asymmetry. *Surgical and Radiologic Anatomy* 25:226-233.

Carey, WB. (1968) Maternal Anxiety and Infantile Colic. Is There a Relationship? *Clinical Pediatrics* 7(10):590-595.

Carey, WB. (1984) "Colic"—primary excessive crying as an infant-environment interaction. *Pediatric Clinics of North America* 31:993-1005.

Carey, WB. (1989) Practical applications in pediatrics. In G. A. Kohnstamm, J. E. Bates and M. K. Rothbart (Eds.), *Temperament in Childhood*. Chichester: Wiley (pp. 405-420).

Carey, WB. & McDevitt, SC. (1978). Revision of the infant temperament questionnaire. *Pediatrics* 61:735-739.

Carmichael, A. & Williams, HE. (1983) Patterns of illness in an infant population in a poor socio-economic status multi-ethnic municipality. *Australian Paediatric Journal* 19:68-72.

Carreiro, JE. (2003) *An Osteopathic Approach to Children.* London: Churchill Livingstone (p.vii).

Carreiro, JE. (2008) *Pediatric Manual Medicine, An osteopathic approach.* London: Churchill Livingstone (p.15).

Casalina, S., Luytena,P., Vliegena, N. & Meursa, P. (2012) The structure and stability of temperament from infancy to toddlerhood: A one-year prospective study. *Infant Behavior & Development* 35:94-108.

Caspi, A., Harrington, HL., Milne, B., Amell, JW., Theodore, RF. & Moffitt, TE. (2003) The human personality shows stability from age 3 to age 26. *Journal of Personality* 71:495-514.

Cavalier, A., Picot, MC., Artiaga, C., Mazurier, E., Amilhau, MO., Froye, E., Captier, G. & Picaud, JC. (2011) Prevention of deformational plagiocephaly in neonates. *Early Human Development* 87:537-543.

Cerritelli, F., Barlafante, G., Renzetti, C., Ricci, F., Loprete, N., Pizzolorusso, G., Fusilli, P. & D'Incecco, C. (2012) Is the placebo effect revealable in newborns? Results from an RCT in osteopathy. *European Journal of Integrative Medicine* 4S:75.

Cerritelli, F., Cicchitti, L., Martelli, M., Barlafante, G., Renzetti, C., Pizzolorusso, G., Lupacchini, M., D'Orazio, M., Marinelli, B., Cozzolino, V., Fusilli, P. & D'Incecco, C. (2015) Osteopathic manipulative treatment and pain in preterms: study protocol for a randomised controlled trial. *Trials* 16:84

Cerritelli, F., Martelli, M., Renzetti, C., Pizzolorusso, G., Cozzolino, V. & Barlafante, G. (2014) Introducing an osteopathic approach into neonatology ward: the NE-O model. *Chiropractic and Manual Therapies* 22:18.

Cerritelli, F., Pizzolorusso, G., Ciardelli, F., La Mola, E., Cozzolino, V., Renzetti, C., D'Incecco, C., Fusilli, P., Sabatino, G. & Barlafante, G. (2013) Effect of osteopathic manipulative treatment on length of stay in a population of preterm infants: a randomized controlled trial. *BioMedical Central Pediatrics* 13:65.

Cezard, JP. (2004). Managing gastro-oesophageal reflux disease in children. *Digestion* 69(Suppl 1):3-8.

Chan, J., Kelley, M. & Khan, J. (1995) Predictors of postnatal head molding in very low birth weight infants. *Neonatal Network* 14:47-52.

Chang, PY., Chang, NC., Perng, DB., Chien, YW. & Huang, FY. (2001) Computer-aided measurement and grading of cranial asymmetry in children with and without torticollis. *Clinical Orthodontics and Research* 4: 200-205.

Chatoor, I. (2002) Feeding disorders in infants and toddlers: diagnosis and treatment. *Child and Adolescent Psychiatric Clinics of North America* 11:163-183.

Chau, K., Lau, E., Greenberg, S., Jacobson, S., Yazdani-Brojeni, P., Verma, N. & Koren, G. (2015) Probiotics for Infantile Colic: A Randomized, Double-Blind, Placebo-Controlled Trial Investigating Lactobacillus reuteri DSM 17938. *The Journal of Pediatrics* 166:74-78.

Chen, MM., Chang, HC., Hsieh, CF., Yen, MF. & Chen, TH. (2005) Predictive model for congenital muscular torticollis: Analysis of 1021 infants with sonography. *Archives of Physical Medication and Rehabilitation* 86(11):2199–2203.

Cheng, JCY. & Au, AW. (1994) Infantile torticollis: a review of 624 cases. *Journal of Pediatric Orthopaedics* 14:802-808.

Cheng, JCY., Tang, SP., Chen, TMK., Wong, MWN. & Wong, EMC. (2000) The clinical presentation and outcomes of treatment of congenital muscular torticollis in infants: A study of 1,086 cases. *Journal of Pediatric Surgery* 35:1091-1096.

Cheng, JCY., Wong, MWN., Tang, SP., Chen, TMK., Shum, SLF. & Wong, EMC. (2001) Clinical determinants of the outcome of manual stretching in the treatment of congenital muscular torticollis in infants. *Journal of Bone and Joint Surgery* 83: 679-687.

Chizawsky, LK. & Findlay, SS. (2005) Tummy time: Preventing unwanted effects of the “Back to Sleep” campaign. *AWHONN Lifelines* 9:382–387.

Cicchetti, DV. & Sparrow, SA. (1981) Developing criteria for establishing interrater reliability of specific items: applications to assessment of adaptive behavior. *American Journal of Mental Deficinecy* 86(2):127-137.

Cioni, G., Bos, AF., Einspieler, C., Ferrari, F., Martijn, A., Paolicelli, PB., Rapisardi, G., Roversi, MF. & Prechtl, HFR. (2000) Early neurological signs in preterm infants with unilateral intraparenchymal echodensity. *Neuropediatrics* 31:240-251.

Clark, R., Hyde, JS., Essex, MJ. & Klein, MH. (1997). Length of maternity leave and quality of mother–infant interactions. *Child Development* 68:364-383.

Clifford, TJ., Campbell, MK., Speechley, KN. & Gorodzinsky, F. (2002) Sequelae of infant colic: evidence of transient infant distress and absence of lasting effects on maternal mental health. *Archives of Pediatrics and Adolescent Medicine* 156:1183-1188.

Cohen, J. (1988) *Statistical power analysis for the behavioral sciences* (2nd ed.). New Jersey: Lawrence Erlbaum.

Cohen Engler, A. Hadash, A., Shehadeh, N. & Pillar, G. (2012) Breastfeeding may improve nocturnal sleep and reduce infantile colic: Potential role of breast milk melatonin. *European Journal of Pediatrics* 171:729-732.

Medoff-Cooper, B., Carey, W. & Mc Devitt, S. (1993) The early infancy temperament questionnaire. *Journal of Development and Behavioral Pediatrics* 14(4):230-235.

Cooper, P. & Murray, L. (1998) Postnatal depression. *British Medical Journal* 316: 1884-1886.

Cozzolino, V., La Mola, E., Ciardelli, F., Cerritelli, F. & Barlafante, G. Impact of OMT on reducing length of stay in a population of pre-term infants. *International Journal of Osteopathic Medicine* 13:104-131.

Costa, R. & Figueiredo, B. (2011) Infant's psychophysiological profile and temperament at 3 and 12 months. *Infant Behavior & Development* 34:270-279.

Costa, AJF., Sarinho, ESC., Motta, MEFA., Gomes, PN., de Oliveira de Melo, SM. & da Silva, GAP. (2011) Allergy to cow's milk proteins: what contribution does hypersensitivity in skin tests have to this diagnosis? *Pediatric Allergy and Immunology* 22:1399-3038.

Cowin, SC. & Doty, SB. (2007) *Tissue mechanics*. New York: Springer.

Cox, J., Holden, J. & Sagovsky, R. (1987) Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786.

Crncec,R., Cooper, E. & Matthey, S. (2010) Treating infant sleep disturbance: Does maternal mood impact upon effectiveness? *Journal of Paediatrics and Child Health* 46:29-34.

Crockenberg, S. & Acredolo, C. (1983). Infant temperament ratings: A function of infants of mothers, or both? *Infant Behavior and Development* 6:61-72.

Cunningham, ML. & Heike, CL. (2007) Evaluation of the infant with an abnormal skull shape. *Current Opinion in Paediatrics* 19(6):645-651.

Danielsson, B. & Hwang, CP. (1985) Treatment of infantile colic with surface active substance (simethicone). *Acta Paediatrica Scandinavica* 74:446-450.

Davis, BE., Moon, RY., Sachs, HC. & Ottolini, MC. (1998) Effects of sleep position on infant motor development. *Pediatrics* 102:1135-1140.

DeGangi, GA., Breinbauer, C., Roosevelt, JD., Porges, S. & Greenspan S. (2000) Prediction of childhood problems at three years in children experiencing disorders of regulation during infancy. *Infant Mental Health Journal* 21:156-175.

DeGangi, GA., DiPietro, JA., Greenspan, SI. & Porges, P. (1991) Psychophysiological characteristics of the regulatory disordered infant. *Infant Behavioral Development* 14:37-50.

DeGangi, GA., Poisson, S., Sickel, R. & Wiener, A. (1995) Therapy Skill Builders. Psychological Corporation; Infant/toddler symptom checklist (ITSC).

DeGangi, GA., Porges, SW. & Sickel, RZ. & Greenspan, SI. (1993) Four-year follow-up of a sample of regulatory disordered infants. *Infant Mental Health Journal* 14:330-343.

De Vries, JIP., Visser, GHA. & Prechtl, HFR. (1982) The emergence of fetal behaviour. Qualitative aspects. *Early Human Development* 7:301-322.

Davids, JR., Wenger, DR. & Mubarak, SJ. (1993) Congenital muscular torticollis: sequela of intrauterine or perinatal compartment syndrome. *Journal of Pediatric Orthopaedics* 13(2):141.

Degenhardt, BF., Darmani, NA., Johnson, JC., Towns, LC., Rhodes, DC., Trinh, C., McClanahan, B. & DiMarzo, V. (2007) Role of osteopathic manipulative treatment in altering pain biomarkers: a pilot study. *Journal of the American Osteopathic Association* 107(9):387-400.

De Greef, E., Hauser, B., Devreker, T., Veereman-Wauters, G. & Vandenplas, Y. (2012). Diagnosis and management of cow's milk protein allergy in infants. *World Journal of Pediatrics* 8(1):19-24.

DeSantis, A., Coster, W. & Bigsby, R. & Lester, B. (2004) Colic and fussing in infancy, and sensory processing at 3 to 8 years of age. *Infant Mental Health Journal* 25:522–539.

De Weerth, C., Fuentes, S. & de Vos, WM. (2013) Crying in infants: On the possible role of intestinal microbiota in the development of colic. *Gut Microbes* 4:416-421.

Dewey, C., Fleming, P. & Golding, J. (1998) Does the supine sleeping position have any adverse effects on the child?II Development in the first 18 months. *Pediatrics* 101:5-9.

Diedrich, O., von Strempel, A., Schloz, M., Schmitt, O. & Kraft, C. (2002) Long-term observation and management of resolving infantile idiopathic scoliosis - A 25-year follow-up. *The Journal of Bone and Joint Surgery* 84(7):1030-1035.

Dobbs, MB. & Weinstein, SL. (1999) Infantile and juvenile scoliosis. *Orthopedic Clinics of North American* 30:331-341.

Dobson, D., Lucassen, PLBJ., Miller, JJ., Vlieger, AM., Prescott, P. & Lewith, G. (2012) *Manipulative therapies for infantile colic (Review)*. The Cochrane Collaboration. London: Wiley & Sons (pp.1-61).

Don, N., Mahon, CMC. & Rossiter, C. (2002) Effectiveness of an individualized multidisciplinary programme for managing unsettled infants. *Journal of Paediatrics and Child Health* 38: 563–567.

Douglas, PS. (2013) Diagnosing gastro-oesophageal reflux disease or lactose intolerance in babies who cry a lot in the first few months overlooks feeding problems. *Journal of Paediatrics and Child Health* 49:e252–e256.

Douglas, PS. (2005). Excessive crying and gastro-oesophageal reflux disease in infants: misalignment of body and culture. *Medical Hypotheses* 64:887-898.

Douglas, PS. & Hill, PS. (2013) Behavioral Sleep Interventions in the First Six Months of Life Do not Improve Outcomes for Mothers or Infants: A Systematic Review. *Journal of Developmental & Behavioral Pediatrics* 34(7):497–507.

Douglas, PS., Hill, PS. & Brodribb W. (2011) The unsettled baby: how complexity science helps *Archives of Disease in Childhood* 96:793–797

Douglas, P. & Hiscock, H. (2010) The unsettled baby: crying out for an integrated, multidisciplinary, primary care intervention. *Medical Journal of Australia* 193:533-536.

Douglas, PS., Mares, RE. & Hill, PS. (2012) Interdisciplinary perspectives on the management of the unsettled baby: key strategies for improved outcomes. *Australian Journal of Primary Health* 18(4):332-338.

Dowling, S. (1977) Seven infants with esophageal atresia: a developmental study. *Psychoanalytic Study of the Child* 32:215–256.

Downey, PA., Barbano, T., Kapur-Wadhwa, R., Sciote, JJ., Siegel, MI. & Mooney, MP. (2006) Craniosacral Therapy: The Effects of Cranial Manipulation on Intracranial Pressure and Cranial Bone Movement. *The Journal of orthopaedic and sports physical therapy* 36(11):845-853.

Dudek-Shriber, L. & Zelazny, S. (2007) The effects of prone positioning on the quality and acquisition of developmental milestones in four-month-old infants. *Pediatric Physical Therapy* 19:48–55.

Duncan, B., McDonough-Means, S., Worden, K., Schnyer, R., Andrews, J. & Meaney, FJ. (2008) Effectiveness of osteopathy in the cranial field and myofascial release versus acupuncture as complementary treatment for children with spastic cerebral palsy: a pilot study. *Journal of the American Osteopathic Association* 108:559-570.

Dunn, P. (1976) Congenital Postural Deformities. *British Medical Bulletin* 32-71.

Dykes, LJ. (1986) The whiplash shaken infant syndrome: What has been learned? *Child Abuse & Neglect* 10:211–221.

Educational Council on Osteopathic Principles of the American Association of Colleges of Osteopathic Medicine (2003). Glossary of osteopathic terminology. *Foundations for osteopathic medicine*. (Ward, R. Ed.). Philadelphia: Lippincott Williams & Wilkins (pp.1229-1253).

Ellett, M., Appleton, M. & Sloan, R. (2009) Out of the Abyss of Colic: A view through the fathers' eyes. *The American Journal of Maternal/Child Nursing* 34(3):164-171.

Emery, C. (1994) The determinants of treatment duration for congenital muscular torticollis. *Physical Therapy* 74:921-929.

Eppinger, H. & Hess, E. (1915) *Vagotonia: A clinical study in vegetative neurology.* New York: Johnson Reprint Corp.

Ernst, E. (2012) Craniosacral therapy: a systematic review of the clinical evidence. *Focus on Alternative and Complementary Therapies* 17(4):197–201.

Evans, DW. (2013) Osteopathic principles: More harm than good? *International Journal of Osteopathic Medicine* 16:46-53.

Evans, RW., Fergusson, DM., Allardyce, RA. & Taylor, B. (1981) Maternal diet and infantile colic in breast-fed infants. *Lancet* 1:1340–1342.

Fabamwo, A., Disu, E., Akinola, O., Adewale, L. & Adewole, L. (2006) Birth Trauma In A Tertiary Maternity Unit In South Western Nigeria. *The Internet Journal of Pediatrics and Neonatology*. 7(2).

Fagen, JW., Ohr, PS., Singer, JM., & Fleckenstein, LK. (1987) Infant temperament and performance on the Bayley scales of infant development at 4, 8, and 12 months of age. *Infant Behavior and Development* 10(4):505-512.

Fawkes, C., Leach, J., Mathias, S. & Moore, AP. (2010) *The standardised data collection project: standardised data collection within osteopathic practice in the UK: development and first use of a tool to profile osteopathic care in 2009.* National Council for osteopathic research, University of Brighton; June 2010.

Fawkes, CA., Leach, CMJ., Mathias, S. & Moore, AP. (2014) A profile of osteopathic care in private practices in the United Kingdom: A national pilot using standardised data collection. *Manual Therapy* 19:125-130.

Feldman, R.; Eidelman, AI.; Sirota, L. & Weller, A. (2002) Comparison of Skin-to-Skin (Kangaroo) and Traditional Care: Parenting Outcomes and Preterm Infant Development Pediatrics 110 (1):16-26.

Ferguson A. (2003) A review of the physiology of cranial osteopathy. *Journal of Osteopathic Medicine* 6:74-88.

Field, T., Sandberg, D., Garcia, R., Vega-Lahr, N., Goldstein, S. & Guy, L. (1985) Pregnancy Problems, Postpartum Depression, and Early Mother-Infant Interactions. *Developmental Psychology* 23(6):1152-1156.

Field, T., Diego, M. & Hernandez-Reif, M (2010) Preterm infant massage therapy research: a review. *Infant Behavior and Development* 33(2):115–124.

Field, T., Diego, M., Hernandez-Reif, M., Figueiredo, B., Schanberg, S. & Kuhn, C. (2007) Sleep disturbances in depressed pregnant women and their newborns. *Infant Behavior and Development* 30:127-133.

Finley, AG., Franck, LS., Grunau, R. & von Baeyer, CL. (2005) Why Children's Pain Matters. *International Association for the Study of Pain Task Force on Acute Pain* XIII(4):1-2.

Fish, M., Stiffer, C. A. & Belsky, J. (1991) Conditions of continuity and discontinuity in infant negative emotionality: newborn to five months. *Child Development*, 62:1525-1537.

Fisher, J. (2011) *Mums with unsettled babies seek emergency help* Interview with Professor Jane Fisher Nursing Review 2011

Fisher, J., Rowe, H., Hiscock, H., Jordan, B., Bayer, J., Colahan A. & Amery, V. (2011) Understanding and responding to unsettled infant behaviour. *A discussion paper for the Australian Research Alliance for Children and Youth.*

Fitzgerald, M. & Walker, S. (2009) Infant pain management: a developmental neurobiological approach. *Nature Clinical Practical Neurology* 5:35-50.

Fleisher, DR. & Barr, R. (2008) Colic. In (M.M. Haith and J.B. Benson) *Encyclopedia of infant and early childhood development*. Pacific Grove, CA: Brooks/Cole Publishing (pp.318-322).

Fleming, AS., Ruble, DN., Flett, GL. & Shaul, DL. (1988) Postpartum Adjustment in First-Time Mothers: Relations Between Mood, Maternal Attitudes, and Mother-Infant Interactions. *Developmental Psychology* 24(1):71-81.

Forsyth, BWC. (1989) Colic and the effect of changing formulas: a double-blind, multiple-crossover study. *Journal of Pediatrics* 115:521-526.

Forsyth, BW. & Canny, PF. (1991) Perceptions of vulnerability 3 ½ years after problems of feeding and crying behavior in early infancy. *Pediatrics* 88:757-763.

Forsyth, BWC., Leventhal, JM. & McCarthy, PL. (1985b) Mothers' perceptions of problems of feeding and crying behaviour. *The American Journal of Diseases of Children* 139:269–272.

Forsyth, BWC., McCarthy, PL. & Leventhal, JM. (1985a) Problems of early infancy, formula changes, and mothers' beliefs about their infants. *The Journal of Pediatrics* 106(6):1012-1017.

Francis-Williams, J. & Yule, W. (1967) The Bayley Infant Scales of Mental and Motor Development: an exploratory study with an English sample. *Developmental Medicine & Child Neurology* 9:391-401.

Freyne, B., Hamilton, K., Mc Garvey, C., Shannon, B., Matthews, TG. & Nicholson AJ. **(**2014) Sudden unexpected death study underlines risks of infants sleeping in sitting devices. *Acta Paediatrica* 103(3):130-132.

Frymann, VM. (1966) Relation of disturbances of craniosacral mechanisms to symptomatology of the newborn: study of 1250 infants. *Journal of American Osteopathic Association* 65:1059-1075.

Frymann VM. (1976) The trauma of birth. *Osteopath Annals* 4:22-31.

Frymann, VM. (1998) *The Collected Papers of Viola M. Frymann, DO. Legacy of Osteopathy to Children* Michigan: Edward Brothers.

Frymann, VM., Carney, RE. & Springall, P. (1992) Effect of osteopathic medicine on neurologic development in children. *Journal of the American Osteopathic Association* 92:729-744.

Fuller, B. (2001) Infant Behaviors as Indicators of Established Acute Pain. *Journal for Specialists in Paediatric Nursing* 6(3):109-115.

Fuller, BF. (1996) *Nursing assessment of infant pain: Model and instrument testing.* Progress Report submitted to the National Institute of Nursing Research, Bethesda, MD.

Fuller, BF. (1998) The process of infant pain assessment. *Applied Nursing Research* 11:62-68.

Fujiwara, T., Barr, RG., Brant, R. & Barr, M. (2011) Infant distress at five weeks of age and caregiver frustration. *The Journal of Pediatrics* 159(3):425-430.

Gabutti, M. & Draper-Rodi, J. (2014) Osteopathic decapitation: Why do we consider the head differently from the rest of the body? New perspectives for an evidence-informed osteopathic approach to the head. *International Journal of Osteopathic Medicine* 17:256-262.

Galbally,M., Lewis, AJ., McEgan, K. Scalzo, K. & Islam, FMA. (2013) Breastfeeding and infant sleep patterns: an Australian population study. *Journal of Paediatrics and Child Health* 49**:**e147-e152.

Garrison, M. & Christakis, A. (2000) A systematic review of treatments for infantile colic. *Pediatrics* 106:184-190.

Gartstein, MA., Knyazev, GG. & Slobodskaya, HR. (2005) Cross-cultural differences in the structure of infant temperament: United States of America (U.S.) and Russia. *Infant Behavior & Development* 28:54–61.

Gartstein, M. & Rothbart MK. (2003) Studying infant temperament via the Revised Infant Behavior Questionnaire. *Infant Behavior & Development* 26:64–86.

Geerdink, JJ., Hopkins, B. and Hoeksma, JB. (1994) The development of head position preference in preterm infants beyond term age. *Developmental Psychobiology* 27:153-168.

General Osteopathic Council. (2015). Osteopathy in practice. Retrieved 16th October 2015, from http://www.osteopathy.org.uk/practice/.

George, L. (2005). Lack of preparedness. Experiences of first-time mothers. *American Journal of Maternal Child Nursing* 30(4):251-255.

Giesbrecht, GF., Dewey, D., the APrON Study Team (2014) The effects of ‘does not apply’ on measurement of temperament with the Infant Behavior Questionnaire—Revised: A cautionary tale for very young infants. *Early Human Development* 90: 627–634.

Gladel, W. (1978) Sleeping position of the infant and development of skeletal disorders. *Zeitschrift für Orthopädie und ihre Grenzgebiete* 116:336-347.

Goldberg S. (1972) Infant care and growth in urban Zambia. *Human Development* 15:77–89.

Golden, KA., Beals, SP., Littlefield, TR. & Pomatto, JK. (1999) Sternocleidomastoid imbalance versus congenital muscular torticollis: their relationship to positional plagiocephaly. *Cleft Palate Craniofacial Journal* 36:256–261.

Goldfeld, SR., Wright, M. & Oberklaid, F. (2003) Parents, infants and health care: Utilization of health services in the first 12 months of life. *Journal of Paediatric and Child Health* 39(4):249-253.

Goldsmith, HH. & Gottesman, F. (1981). Origins in variation in behavioral style. *Child Development* 52, 91-103.

Goldsmith, HH., & Rothbart, MK. (1991). *Contemporary instruments for assessing early temperament by questionnaire and in the laboratory*. In A. Angleitner & J. Strelau (Eds.), Explorations in temperament: International perspectives on theory and measurement. New York: Plenum.

Good, C. & Walker, G. (1984) The hip in the Moulded Baby Syndrome. *The Journal of Bone and Joint Surgery* 66(4):491-492.

Goodlin-Jones, BL., Burnham, MM., Gaylor, EE. & Anders, TF. (2001) Night waking, sleep-wake organization, and self-soothing in the first year of life. *Journal of Developmental and Behavioral Pediatrics* 22:226–33.

Gormally, S. & Barr, R. (1997). Of clinical pies and clinical clues: A proposal for a clinical approach to complaints of early crying and colic. *Ambulatory Child Health* 3:137-153.

Gottlieb MS (1993) Neglected Spinal Cord, Brain Stem and Musculoskeletal Injuries Stemming from Birth Trauma. *Journal of Manipulative and Physiologic Therapeutics* 16(8):537-543.

Graham, JM Jr., de Saxe, M. & Smith, DM. (1979) Sagittal craniostenosis: fetal head constraint as one possible cause. *Journal of Pediatrics* 95:747-750.

Green, C., Martin, C., Bassett, K. & Kazajian, A. (1999) *A systematic review and critical appraisal of the scientific evidence on craniosacral therapy.* British Columbia Office of Health Technology Assessment, The University of British Columbia.

Gudmundsson, G. (2010) Infantile colic: is a pain syndrome. *Medical Hypothesis* 75:528-529.

Guedeney, A. & Fermanian, J. (2001). A validity and reliability study of assessment and screening for sustained withdrawal reaction in infancy: The alarm distress baby scale. *Infant Mental Health Journal* 22(5):559–575.

Gunn, J., Lumley, J. & Young D. (1996) Visits to medical practitioners in the first six months of life. *Journal of Paediatric and Child Health* 32:162-166.

Gupta, P., Foster, J., Crowe, S., Papay, F., Luciano, M. & Traboulsi, E. (2003) Opthalmologic Findings in Patients with Nonsyndromic Plagiocephaly. *Journal of Craniofacial Surgery* 14:529-532.

Guyer, B., Ma, S., Grason, H., Frick, KD., Perry, DF., Sharkey, A. & McIntosh, J. (2009) Early childhood health promotion and its life course health consequences. *Academic Pediatrics* 9(3):142-149.

Guyer, J., Millward, LJ. & Berger, I. (2012) Mothers' breastfeeding experiences and implications for professionals. *British Journal of Midwifery* 20(10):724-733.

Hall, RT., Mercer, AM., Teasley, SL., McPherson, DM., Simon, SD., Santos, SR., Meyers, BM. & Hipsh, NE. (2002) A breastfeeding assessment score to evaluate the risk for cessation of breast-feeding by 7 to 10 days of age. *Journal of Pediatrics* 141(5):659–664.

Hamanishi, C. & Tanaka, S. (1994) Turned head adducted hip truncal curvature syndrome. *Archives of Disease in Childhood* 70:515-519.

Hanten, W., Olson, S., Hodson, J., Imler, V., Knab ,V. & Magee, J. (1999) The effectiveness of CV-4 and resting position techniques on subjects with tension-type headaches. *The Journal of manual & manipulative therapy* 7:64-70.

Hart, LM. (1918) Obstetrical practise. *Journal of the American Osteopathic Association* 609-614.

Haas, SV. (1918) The hypertonic infant, the curative action of atropine on certain of its manifestations. *American Journal of Diseases of Children* 15:323-335.

Hawk, C., Khorsam, R., Lisi, AJ. Ferrance, RJ. & Willard Evans, M. (2007) Chiropractic Care for Nonmusculoskeletal Conditions: A Systematic Review with Implications for Whole Systems Research. *The Journal of Alternative and Complementary Medicine* 13(5):491–512.

Hawthorne, J. (2004) Training health professionals in the Neonatal Behavioral Assessment Scale (NBAS) and its use as an intervention. *The Signal, Newsletter of the World Association for Infant Mental Health* 12(3&4):1-5.

Hayden, C. & Mullinger, B. (2006) A preliminary assessment of the impact of cranial osteopathy for the relief of infantile colic. *Complementary Therapies in Clinical Practice* 12:83-90.

Hayes, MJ., McCoy, SK., Fukumizu, M., Wellman, JD. & DiPietro, JA. (2011) Temperament and sleep–wake behaviour from infancy to toddlerhood. *Infant and Child Development* 20(5):495-508.

Hein, HA. & Pettit, SF. (2001) Back to Sleep: Good advise for parents but not for hospitals? *Pediatrics* 107:537-539

Heine, RG., Jaquiery, A., Lubitz, L., Cameron, BJ. & Catto-Smith, AG. (1995) Role of gastro-oesophageal reflux in infant irritability. *Archives of Disease in Childhood* 73:121–125.

Heine, RG., Cameron, DJ., Chow, CW., Hill, DJ. & Catto-Smith, AG. (2002) Esophagitis in distressed infants: poor diagnostic agreement between esophageal pH monitoring and histopathologic findings. *Journal of Pediatrics* 140:14-9.

Heine, RG., Jordan, B., Lubitz, L., Meehan, M, Catto-Smith, AG. (2006) Clinical predictors of pathological gastro-oesophageal reflux in infants with persistent distress. *Journal of Paediatric and Child Health* 42(3):134-139.

Helseth, S. & Begnum, S. (2002). A comprehensive definition of infant colic: parents' and nurses' perspectives. *Journal of Clinical Nursing* 11(5):672-680.

Hemmi, MH., Wolke, D. & Schneider, S. (2011) Associations between problems with crying, sleeping and/or feeding in infancy and long-term behavioural outcomes in childhood: a meta-analysis. *Archives of Disease in Childhood* 96:622–629.

Henley, CE., Ivins, D., Mills, M., Wen, FK. & Benjamin, BA (2008) Osteopathic manipulative treatment and its relationship to autonomic nervous system activity as demonstrated by heart rate variability: a repeated measures study. *Osteopathic Medicine and Primary Care* 5(2):7.

Henry, SM. (2004). Discerning differences: gastroesophageal reflux and gastroesophageal reflux disease in infants. *Advances in Neonatal Care* 4(4):235-247.

Hewlett, BS., Lamb, ME., Shannon, D., Leyendecker, B. & Scholmerich, A. (1998) Culture and early infancy among Central African foragers and farmers. *Developmental Psychology* 34:653–661.

Hewson, P., Oberklaid, F. & Menahem, S. (1987) Infant colic, distress, and crying. *Clinical Pediatrics* 26:69-76.

Hide, DW. & Guyer, BM. (1982) Prevalence of infant colic. *Archives of Disease in Childhood* 57:559-560.

Hill, DJ., Firer, MA., Shelton, MJ, & Hoskins, CS. (1986) Manifestations of milk allergy in infancy: clinical and immunologic findings. *Journal of Pediatrics* 109:270-276.

Hill, DJ., Hudson, IL., Sheffield, LJ., Shelton, MJ., Menahem, S. & Hosking, CS. (1995) A low allergen diet is a significant intervention in infantile colic: Results of a community-based study. *Journal of Allergy and Clinical Immunology* 95(6):886-892.

Hill, DJ., *Menahem, S.*, *Hudson*, I., IN Sheffield, L., Shelton, M., Oberklaid, F. & Hosking, CS. *(1992) Charting infant distress*: an aid to defining colic. *Journal of Pediatrics* 121:755-758.

Hill, DJ., Roy, N., Heine, RG., Hosking, CS., Francis, DE., Brown, J., Speirs, B., Sadowsky, J. & Carlin, JB. (2005) Effect of a low-allergen maternal diet on colic among breastfed infants: A randomized, controlled trial. *Pediatrics* 116:709-715.

Hinton, DR., Becker, LE., Muakkassa, KF. & Hoffman, HJ. (1984) Lambdoidal synostosis. Part 1: The lambdoid suture: normal development and pathology of “synostosis”. *Journal of Neurosurgery* 61:333-339.

Hipperson, AJ. (2004) Chiropractic management of infantile colic. *Clinical Chiropractic* 7(4):180-186.

Hiscock, H. (2010) Rock-a-bye baby? Parenting and infant sleep. *Sleep Medical Review* 14:85-87.

Hiscock, H. & Jordan B. (2004) Problem crying in infancy. *Medical Journal of Australia, Practice Essentials - Paediatrics*. 181(9):507-12.

Hogdall, C; Vestermark, V; Birch, M; Plenov, G. & Loftager-Larsen, K. (1991) The significance of pregnancy, delivery and post-partum factors for the development of infantile colic. *Journal of Perinatal Medicine* 19:251-257.

Holsti, L. & Grunau, RE. (2007) Initial validation of the behavioural indicators of infant pain (BIIP). *Pain* 132:264-272.

Holt, K. (1960) Early motor development: posturally induced variations. *Journal of Pediatrics* 57:571-575.

Hopkins, B., Lems, W., Janssen, B. & Butterworth, G. (1987) Postural and motor asymmetries in newlyborns. *Human Neurobiology* 23:39-53.

Hort, KP. (1992) Health problems and service use by parents of normal infants in the first 6 months of life. *Journal of Paediatrics and Child Health* 28:286-290.

Høst, A., Jacobsen, HP., Halken, S. & Holmenlund, D. (1995) The natural history of cow's milk protein allergy/intolerance. European Journal of Clinical Nutrition 49(Suppl 1):13-18.

Høst, A. (2002) Frequency of cow's milk allergy in childhood. *Annals of Allergy, Asthma and Immunology* 89(Suppl 1):33-37.

Høst, A., Husby, S., Hansen, LG. & Osterballe, O. (1990) Bovine beta-lactoglobulin in human milk from atopic and non-atopic mothers. Relationship to maternal intake of homogenized and unhomogenized milk. *Clinical and Experimental Allergy* 20:383-387.

Hoult, I., MacLennan, A. & Carrie, L. (1977) Lumbar epidural analgesia in labour: relation to fetal malposition and instrumental delivery. *British Medical Journal* 1:14-16.

Howard, CR., Lanphear, N., Lanphear, BP., Eberly, S. & Lawrence, RA. (2006) Parental responses to infant crying and colic: the effect on breastfeeding duration. *Breastfeeding Medicine* 1(3):146-155.

Howell, EA., Mora, P. & Leventhal, H. (2006) Correlates of early postpartum depressive symptoms. *Maternal and Child Health Journal* 10:149-157.

Huang, MH., Gruss, JS., Clarren, SK., Mouradian, WE., Cunningham, ML., Roberts, TS., Loeser, JD. & Cornell, CJ. (1996) The differential diagnosis of posterior plagiocephaly: true lambdoid synostosis versus positional molding. *Plastic and Reconstructive Surgery* 98:765–774, discussion 775-776.

Hughes, S. & Bolton, J. (2002) Is chiropractic an effective treatment of infantile colic? *Archives of Disease in Childhood* 86:382-384.

Hunziker, UA. & Barr, RG. (1986) Increased carrying reduces infant crying: a randomized controlled trial. *Pediatrics* 77:641-648.

Hurry, J., Bowyer, J. & St. James-Roberts, I. (1991) *The development of infant crying and its relationship to sleep-waking organisation.* Paper presented at the Biennial Meeting of the Society for Research in Child Development, Seattle, Washington.

Hutchison, BL., Hutchison, LA., Thompson, JM. & Mitchell, EA. (2004) Plagiocephaly and brachycephaly in the first two years of life: a prospective cohort study. *Pediatrics* 114:970-980.

Hutchison, BL., Stewart, AW., De Chalain, TB. & Mitchell, EA. (2010) A randomized controlled trial of positioning treatments in infants with positional head shape deformities. *Acta Paediatrica* 99:1556-1560.

Hutchison, BL., Thompson, JM. & Mitchell, EA. (2003) Determinants of nonsynostotic plagiocephaly: a case-control study. *Pediatrics* 112(4):e316.

Hyams, JS., Geertsma, MA., Etienne, NE. & Treem, WR. (1989) Colonic hydrogen production in infants with colic. *Journal of Pediatrics* 115:592-594.

Hylton, N. (1997) Infants with torticollis: the relationship between asymmetric head and neck positioning and postural development. *Physical & Occupational Therapy in Pediatrics* 17:91-117.

Hyman, PE., Milla, PJ., Benninga, MA., Davidson, GP., Fleisher, DF. & Taminiau, J. (2006) Childhood functional gastrointestinal disorders: neonate/toddler. *Gastroenterology* 130:1519-1526.

Iacono, G., Carroccio, A., Montalto, G., Cavataio, F., Bragion, E., Lorello, D. Balsamo, V. & Notarbartolo, A. (1991) Severe infantile colic and food intolerance: a long-term prospective study. *Journal of Pediatric Gastroenterology and Nutrition* 12:332-335.

IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.

Illingworth, RS. (1985) Infantile colic revisited. *Archives of Disease in Childhood* 60: 981-985.

Jäkel, A. & von Hauenschild, P. (2011) Therapeutic effects of cranial osteopathic manipulative medicine: a systematic review. Journal of the American Osteopathic Association 111:685-693.

Jakobsson, I. & Lindberg, T. (1978) Cows milk as a cause of infantile colic in breast-fed infants. *Lancet* 2:437-439.

James, JIP. (1951) Two curve patterns in idiopathic structural scoliosis. *Journal of Bone and Joint Surgery* 33(B):399-406.

James, JIP. (1975) The management of infants with scoliosis. *Journal of Bone and Joint Surgery* Br57:422-429.

Jantz, JW., Blosser, CD. & Fruechting, LA. (1997) A motor milestone change noted with a change in sleep position. *Archives in Pediatric and Adolescent Medicine* 151: 565-568.

Jennings, JT., Sarbaugh, BG. & Payne, NS. (2005) Conveying the message about optimal infant positions. *Physical & Occupational Therapy in Pediatrics* 25:3-18.

Joganic, JL., Lynch, JM., Littlefield, TR. & Verrelli, BC. (2009) Risk factors associated with deformational plagiocephaly. *Pediatrics* 124:e1126-e1133.

Johnson, JD., Cocker, K. & Chang, E. (2015) Infantile Colic: Recognition and Treatment. *American Family Physician* 92(7):577-582.

Jordan, B., Heine, RG., Meeham, M., Catto-Smith, AG. & Lubitz L. (1999) The irritable infant intervention study: Effect of anti-reflux medication and infant mental health intervention on persistent infant irritability. *Proceedings of the Division of Paediatrics Annual Scientific Meeting, Perth*.

Jorup, S. (1952) *Colonic hyperperistalsis in neurolabile infants*. Acta Pediatrica 85:1-110.

Joyce, P. & Clark, C. (1996) The use of craniosacral therapy to treat gastroesophageal reflux in infants. *Infants Young Child* 9:51-57.

Juniper, EF. (2009) Validated questionnaires should not be modified. *European Respiratory Journal* 34:1015–1017.

Kagan, J. (1998). Biology and the child. In W. Damon & N. Eisenberg (Eds.), *Handbook of child psychology: Vol. 3. Social, emotional and personality development* (5th ed.). New York: Wiley (pp. 177-235).

Kagan, J., Snidman, N. & Arcus, D. (1993). On the temperamental categories of inhibited and uninhibited children. In K.H. Rubin and J.B. Asendorpf (Eds.), *Social withdrawal, inhibition, and shyness in childhood.* Hillsdale, NJ: Lawrence Erlbaum Associates (pp.19-28).

Kalra, R. & Walker, ML. (2012) Posterior plagiocephaly. *Childs Nervous System* 28:1389–1393

Kane, AA., Mitchell, LE., Craven, KP. & March, JL. (1996) Observations on a recent increase in Plagiocephaly without Synostosis. *Pediatrics* 97(6):877-885.

Kawahara, H., Dent, J. & Davidson, G. (1997) Mechanisms responsible for gastroesophageal reflux in children. *Gastroenterology* 113:399–408.

Kawahara, H., Dent, J., Davidson, G. & Okada, A. (2001) Relationship between straining, transient lower esophageal sphincter relaxation, and gastroesophageal reflux in children. *American Journal of Gastroenterology* 96:2019–2025.

Keefe, MR., Lobo, ML., Froese-Fretz, A., Kotzer, AM., Barbosa, GA. & Dudley, WN. (2006) Effectiveness of an intervention for colic. *Clinical Pediatrics* 45:123-133.

Keener, MA. & Zeanah, CHATF. (1988) Infant temperament, sleep organization, and nighttime parental intervention. *Pediatrics* 81(6):762-771.

Keesen, W., Crow, A. & Hearn, M. (1993) Proprioceptive accuracy in idiopathic scoliosis. *Spine* 17:149-155.

Kelly, KM., Littlefield, TR., Pomatto, JK., Manwaring, KH. & Beals, SP. (1999) Cranial growth unrestricted during treatment of deformational plagiocephaly. *Pediatric Neurosurgery* 30:193–199.

Kelly, KM., Littlefirld, TR., Pornatto, JK., Ripley, CE., Beals, SP. & Joganic, EF. (1999) Importance of early recognition and treatment of deformational plagiocephaly with orthotic cranioplasty. *Cleft Palate-Craniofacial Journal* 36:127-130.

Kerr, SM., Jowett, SA. & Smith, LN. (1996) Preventing sleep problems in infants: a randomised controlled trial. *Journal of Advanced Nursing* 24:928-942.

Kerwin, ME. (1999) Empirically supported treatments in pediatric psychology: severe feeding problems. *Journal of Pediatric Psychology* 24:193-214.

Khoshoo, V., Ross, G., Brown, S. & Edell, D. (2000) Smaller volume, thickened formulas in the management of gastroesophageal reflux in thriving infants. *Journal of Pediatric Gastroenterology Nutrition* 31:554-556.

King, HH., Tettambel, MA., Lockwood, MD., Johnson, KH., Arsenault, DA. & Quist, R. (2003) Osteopathic manipulative treatment in prenatal care: a retrospective case control design study. *Journal of the American Osteopathic Association* 103:577–582.

Klackenberg, EP., Elfving, B., Haglund-Akerlind, Y. & Carlberg, EB. (2005) Intra-rater reliability in measuring range of motion in infants with congenital muscular torticollis. *Advances in Physiotherapy* 7:84-91.

Kliegman, RM., Behrman, RE., Jenson, HB. & Stanton, BF (2007) *Nelsons Textbook of Pediatrics* (18^{th} ed.). Philadelphia: Saunders Elsevier.

Klougart, N., Nilsson, N & Jaconsen, J. (1989) Infantile colic treated by chiropractors: a prospective study of 316 cases. *Journal of Manipulative and Physiological Therapies* 12(4):281-288.

Koe, S, Price, B., May, S., Kyne, L., Keenan, P., McKay, M. & Nicholson, AJ. (2010) Medical, social and societal issues in infants with abusive head trauma. *Irish Medical Journal* 103(4):102-105.

Kohlhoff, J., Barnett, B. & Eapen, V. (2015) Adult separation anxiety and unsettled infant behavior: Associations with adverse parenting during childhood and insecure adult attachment. *Comprehensive Psychiatry* 61:1-9.

Koletzko, S., Niggemann, B., Arato, A., Dias, JA., Heuschkel, R., Husby, S., Mearin, ML., Papadopoulou, A., Ruemmele, FM., Staiano, A., Schäppi, MG. & Vandenplas, Y. (2012) Diagnostic approach and management of cow's milk protein allergy in infants and children: ESPGHAN GI Committee practical guidelines. *Journal of Pediatric Gastroenterology and Nutrition* 55:221-229.

Konishi, Y., Mikawa, H. & Suzuki, J. (2002) Asymmetrical head turning of preterm infants: some effects on later postural and functional literalities. *Developmental Psychobiology* 40:1-13.

Kordestani, RK. & Panchal, J. (2006) Neurodevelopment delays in children with deformational plagiocephaly. *Plastic and Reconstructive Surgery* 118:808-809.

Kotelnikova, Y., Olino, TM., Klein, DN., Kryski, KR. & Hayden, EP. (2015) Higher and Lower-Order Factor Analyses of the Children's Behavior Questionnaire in Early and Middle Childhood. *Psychological Assessment*. Advance online publication.

Kotzampaltiris, PV., Chou, KJ., Wall, SP. & Crain, EF. (2009) The Cranial Rhythmic Impulse and Excessive Crying of Infancy. *The Journal of Alternative and Complementary Medicine* 15(4):1-5.

KPMG. (2011) *How do osteopaths practise? General Osteopathic Council*. http://www.osteopathy.org.uk/uploads/how_do_osteopaths_practise_kpmg_report a_ozone.pdf.

Kurtoglu, S., Uzum, K., Hallac, IK. & Coskum, A. (1997) 5-hydroxy-3-indole acetic acid levels in infantile colic: is serotoninergic tonus responsible for this problem? *Acta Paediatrica* 86:764-765.

Lam, P., Hiscock, H. & Wake, M. (2003) Outcomes of Infant Sleep Problems: A Longitudinal Study of Sleep, Behavior, and Maternal Well-Being. *Pediatrics* 111(3):203-207.

Lam, J., Barr, RG., Catherine, N., Tsui, H., Hahnhaussen, CL., Pauwels, J. & Brant, R. (2010) Electronic and paper diary recording of infant and caregiver behaviors. *Journal Of Developmental And Behavioral Pediatrics* 31(9):685-693.

Landgren, K., Kvorning, N. & Hallstmm, I. (2010) Acupuncture reduces crying in infants with infantile colic: a randomised, controlled, blind clinical study. *Acupuncture in Medicine* 28:174-179.

Landis, JR. & Koch, GG. (1977) The measurement of observer agreement for categorical data. *Biometrics* 33(1):159-174.

Laughlin, J., Luerssen, TG. & Dias, MS. (2011) Committee on Practice and Ambulatory Medicine, Section on Neurological Surgery. Prevention and management of positional skull deformities in infants. *Pediatrics.* 128:1236-1241.

Lee, K. (1994). The crying pattern of Korean infants and related factors. *Developmental Medicine and Child Neurology* 36:601-607.

Lehtonen, L., Gormally, S. & Barr, RG. (2000) Clinical pies' for etiology and outcome in infants presenting with early increased crying. In R. Barr, B. Hopkins and J. Green (Eds.), *Crying as a sign, a symptom, and a signal*. London: MacKeith Press (pp.67-95).

Lehtonen, L. & Korvenranta, MD. (1995) Infantile Colic, Seasonal Incidence and Crying Profiles. *Archives of Pediatrics & Adolescent Medicine* 149:533-536.

Lehtonen, L., Korhonen, T. & Korvenranta, H. (1994a) Temperament and sleeping patterns in colicky infants during the first year of life. *Journal of Developmental and Behavioural Pediatrics* 15:416-420.

Lehtonen, L., Svedstrom, E. & Korvenranta, H. (1994b) Gallbladder hypocontractability in infantile colic. *Acta Paediatrica* 83:1174-1177.

Lessard, S., Gagnon, I. & Trottier, N. (2011) Exploring the impact of osteopathic treatment on cranial asymmetries associated with nonsynostotic plagiocephaly in infants. *Complementary Therapies in Clinical Practice* 17:193-198.

Leung, AK. (1987) Infantile colic. *American Family Physician* 36:153-156.

Leung, AK., Chan, PY., Cho, HY. & Choi, MC. (1997) An updated review of infantile colic. *Canadian Journal of Clinical Medicine* 4(10):16-19.

Leung, AK. & Lemay, JF. (2004) Infantile colic: a review. *The Journal of the Royal Society for the Promotion of Health* 124:162-166.

Levine, MG., Holroyde, J., Woods, JR., Siddiqi, TA., Scott, M. & Miodovnik, M. (1984) Birth trauma: Incidence and predisposing factors. *Obstetrics and Gynecology* 63(6):792–795.

Levitt, MD. (1969) Production and excretion of hydrogen gas in man. *New England Journal of Medicine* 281:122-127.

Levitt, CJ., Smith, WL., & Alexander, RC.(1996) Abusive head trauma. In R.M.Resse (Ed.), *Childabuse: Medical diagnosis and management* Baltimore: Williams and Wilkins (pp. 1–22).

Levitzky, S. & Cooper, R. (2000) Infant colic syndrome: maternal fantasies of aggression and infanticide. *Clinical Paediatrics* 39:395-400.

Licciardone, JC., Stoll, ST., Fulda, KG., Russo, DP., Siu, J., Winn, W. & Swift J. (2003) Osteopathic Manipulative Treatment for Chronic Low Back Pain, A Randomized Controlled Trial. *Spine* 28(13):1355-1362.

Licciardone, JC. (2004) The Unique Role of Osteopathic Physicians in Treating Patients With Low Back Pain. *Journal of the American Osteopathic Association* 104(11 Suppl 8):S13-8.

Licciardone, JC., Brimhall, AK. & King, LN. (2005) Osteopathic manipulative treatment for low back pain: a systematic review and metaanalysis of randomized controlled trials. *BMC Musculoskeletal Disorders* 6:43.

Licciardone, JC., Buchanan, S., Hensel, KL., King, HH., Fuld, KG. & Stoll, ST. (2010) Osteopathic manipulative treatment of back pain and related symptoms during pregnancy: a randomised controlled trial. *American Journal of Obstetrics and Gynecology* 202:43.

Liebman, WM. (1981) Infantile colic: Association with lactose and milk intolerance. *Journal of the American Medical Association* 245:732-736.

Liederman, J. & Coryell, J. (1982) The origin of left hand preference: pathological and non-pathological influences. *Neuropsychologia* 20(6):721-725.

Lim, KW. (2006) Infantile colic: A critical appraisal of the literure from an osteopathic perspective. *International Journal of Osteopathic Medicine* 9:94-102.

Linder, N., Linder, I., Fridman, E., Kouadio, F., Lubin, D., Merlob, P., Yogev, Y. & Melamed, N. (2013) Birth trauma – risk factors and short-term neonatal outcome. *The Journal of Maternal-fetal and neonatal medicine* 26(15):1491-1495.

Littlefield, TR., Beals, SP., Manwaring, KH., Pomatto, JK., Joganic, EF., Golden, KA. & Ripley, CE. (1998) Treatment of craniofacial asymmetry with dynamic orthotic cranioplasty. *Journal of Craniofacial Surgery* 9:11-17

Littlefield, TR., Kelly, KM., Pomatto, JK. & Beals, SP. (1999) Multiple-birth infants at higher risk for development of deformational plagiocephaly. *Pediatrics* 103:565-569.

Littlefield, TR., Kelly, KM., Pomatto, JK. & Beals, SP. (2002) Multiple-birth infants at higher risk for development of deformational plagiocephaly: II. Is one twin at greater risk? *Pediatrics* 109:19-25.

Lloyd, J. (2002). Cranial osteopathy in the treatment of infants and children. *Kiwi Parent* 42-45.

Lloyd-Roberts, GC. & Pilcher, MF. (1965) Structural idiopathic scoliosis in infancy. *The Journal of Bone and Joint Surgery* (Br) 47(B):520-523.

Losee, JE. & Mason, AC. (2005) Deformational plagiocephaly: Diagnosis, prevention and treatment. *Clinics in Plastic Surgery* 32:53-64.

Lothe, L, & Lindberg, T. (1989) Cow's Milk Whey Protein Elicits Symptoms of Infantile Colic in Colicky Formula Fed Infants: A Double-Blind Crossover Study. *Pediatrics* 83:262-266.

Lothe, L., Ivarsson, SA., Ekman, R. & Lindberg, T. (1990a) Motilin and infantile colic. A prospective study. *Acta Paediatrica Scandinavia* 79:410-416.

Lothe, L., Lindberg, T. & Jakobsson, I. (1982) Cow's milk formula as a cause of infantile colic. A double blind study. *Pediatrics* 70:77.

Lothe, L., Lindberg, T. & Jakobsson, I. (1990b) Macromolecular absorption in Infants with Infantile Colic. *Acta Paediatrica* 79:417-421.

Loveday, BP. & de Chalain, TB. (2001) Active counterpositioning or orthotic device to treat positional plagiocephaly? *Journal of Craniofacial Surgery* 12:308-313.

Lozoff, B., Wolf, AW. & Davis, NS. (1985) Sleep problems seen in pediatric practice. *Pediatrics* 75:477-83.

Lozinsky, AC. & de Morais, MB. (2014) Eosinophilic colitis in infants. *Journal of Pediatrics* 90(1):16-21.

Lucassen, P., Assendelft, W., Gubbels, J., van Eijk, J., van Geldrop, W. & Knuistingh Neven, A. (1998) Effectiveness of treatments for infantile colic: systematic review. *British Medical Journal* 316:1563-1569.

Ludwig, S. (1984). Shaken Baby Syndrome: A review of 20 cases. *Annals of Emergency Medicine* 13:104-107.

Macedo, A., Marques, M., Bos, S., Maia, BR., Pereira, T., Soares, MJ., Valente, J. Gomes, AA., Nogueira, V. & Azevedo, MH. (2011) Mother's personality and infant temperament. *Infant Behavior & Development* 34:552-568.

Magoun, HI. (1951) *Osteopathy in the cranial field.* Kirksville, MO: The Journal Printing Company (p. 203).

Magoun, HI. (1966) *Osteopathy in the Cranial Field* (2nd ed.) Kirksville, MO: The Journal Printing Company.

Majnemer, A. & Barr, RG. (2005) Influence of supine sleep positioning on early motor milestones acquisition. *Developmental Medicine & Child Neurology* 47:370-376.

Martin, CM. & Kasperski, J. (2010) Developing interdisciplinary maternity services policy in Canada. Evaluation of a consensus workshop. *Journal of Evaluation in Clinical Practice* 16:238-245.

Matheson, I. & Rivrud, GN. (1989) The effect of smoking on lactation and infantile colic. *Journal of the American Medical Association* 261:42-43.

Mathisen, B., Worrall, L., Masel, J., Wall, C. & Shepherd, RW. (1999) Feeding problems in infants with gastro-oesophageal reflux disease: a controlled study. *Journal Paediatric and Child Health* 35:163-169.

Mau, H. (1981) The changing concept of infantile scoliosis. *International Orthopaedics* 5:131-137.

Mavrogenis, AF., Mitsiokapa, EA., Kanellopoulos, AD., Ruggieri, P. & Papagelopoulos, PJ. (2011) Birth fracture of the clavicle. *Advances in Neonatal Care* 11(5):328-331.

Mayberry, LJ. & Affonso, DD. (1993) Infant temperament and postpartum depression: a review. *Health Care for Women International* 14:201-211.

McCallum, SM., Rowe, HJ., Gurrin, L., Quinlivan, JA., Rosenthal, DA. & Fisher JR. (2011) Unsettled infant behaviour and health service use: a cross-sectional community survey in Melbourne, Australia. *Journal of Paediatrics and Child Health* 47(11):818-823.

McGrath, JM., Records, K. & Rice, M. (2008) Maternal depression and infant temperament characteristics. *Infant Behavior & Development* 31(1):71-80.

McKinney, CM., Cunningham, ML., Holt, VL., Leroux, B. & Starr, JR.(2008) Characteristics of 2733 cases diagnosed with deformational plagiocephaly and changes in risk factors over time. *The Cleft Palate-Craniofacial Journal* 45:208–216.

McMahon, C., Barnett, B., Kowalenko, N., Tennant, C. & Don, N. (2001) Post-natal depression, anxiety and unsettled infant behaviour. *Australian & New Zealand Journal of Psychiatry* 35:581–588.

McManus,C., Davison, A. & Armour, J. (2013) Multilocus genetic models of handedness closely resemble single-locus models in explaining family data and are compatible with genome-wide association studies *Annals of the New York Academy of Sciences* 88:48–58.

McMaster, MJ. (1983) Infantile idiopathic scoliosis: can it be prevented? *Journal of Bone and Joint Surgery (Am*) 65:612-617.

McPartland, JM. & Skinner, E. (2005) The biodynamic model of osteopathy in the cranial field. *EXPLORE: The Journal of Science & Healing* 1:21-32.

McVeigh, C. (1997) Motherhood experiences from the perspective of first-time mothers. *Clinical Nursing Research* 6(4):335-348.

Mead, N. & P. Bower (2000). Patient-centredness: a conceptual framework and review of the empirical literature. *Social Science & Medicine* 51(7):1087-1110.

Meltzer, KR. & Standley, PR. (2007) Modeled repetitive motion strain and indirect osteopathic manipulative techniques in regulation of human fibroblast proliferation and interleukin secretion. *Journal of the American Osteopathic Association* 107(12):527–536.

Merwat, SN. & Spechler, SJ. (2009) Might the use of acid-suppressive medications predispose to the development of eosinophilic esophagitis? *American Journal of Gastroenterology* 104:1897-1902.

Metcalf, TJ., Irons, TG., Sher, LD. & Young, PC. (1994) Simethicone in the treatment of infantile colic: a randomized, placebo-controlled, multicentre trial. *Pediatrics* 94:29-34.

Messer, D. & Richards, M. (1993) The development of sleeping difficulties. In: I. St James-Roberts, G. Harris & D. Messer (Eds.), *Infant Crying, Feeding and Sleeping: Development, Problems and Treatments.* London: Harvester Wheatsheaf (pp. 150-173).

Miles, J. & Shevlin, M. (2001). *Applying Regression and Correlation: A Guide for Students and Researchers*. London: Sage.

Milgrom, J., Westley, DT. & McCloud, PI. (1995) Do infants of depressed mothers cry more than other infants? *Journal of Paediatric and Child Health* 31: 218–221.

Milidou, I, Søndergaard Lindhard, M., Søndergaard, C., Olsen, J. & Brink Henriksen, T. (2015) Developmental Coordination Disorder in Children with a History of Infantile Colic. *Journal of Pediatrics* 167:725-730.

Miller, JE. (2014) Effects of musculoskeletal dysfunction in excessive crying syndromes of infancy. *eprints.bournemouth.ac.uk/21490/1/Miller.Thesis.PDF.*

Miller, AR. & Barr RG. (1991) Infantile colic. Is it a gut issue? *Pediatric Clinics of North America* 38:1407-1423.

Miller, A., Barr, R. & Eaton, W. (1993) Crying and motor behaviour of six-week-old infants and postpartum maternal mood. *Pediatrics* 92:551-558.

Miller, J., Fontana, M., Jernlas, K. & Olofsson, H. (2013) Risks and rewards of early musculoskeletal assessment: An evidence-based case report. *British Journal of Midwifery* 21(10):736-743.

Miller, LC., Johnson, A., Duggan, L. & Behm, M (2011) Consequences of the "Back to Sleep" Program in Infants. *Journal of Pediatric Nursing* 26(4):364-368.

Miller, RI. & Clarren, SK. (2000) Long-term developmental outcomes in patients with deformational plagiocephaly. *Pediatrics* 105(2):e26.

Miller, JJ., McVeagh, P., Fleet, GH., Petocz, P. & Brand, JC. (1989) Breath hydrogen excretion in infants with colic. *Archives of Disease in Childhood* 64:725-729.

Miller, JJ., McVeagh, P., Fleet, GH., Petocz, P. & Brand, JC. (1990) Effect of yeast lactase enzyme on "colic" in infants fed human milk. *Journal of Pediatrics* 117:261-263.

Miller, J., Miller, L., Sulesund, A-K. & Yevtushenko, A. (2009) Contribution of chiropractic therapy to resolving suboptimal breastfeeding: A case series of 114 infants. *Journal of Manipulative and Physiologic Therapeutics* 32(8):670-674.

Miller-Loncar, C., Bigsby, R., High, P., Wallach, M. & Lester, B. (2004) Infant colic and feeding difficulties. *Archives of Disease in Childhood* 89:908-912.

Mills, MV., Henley, CE., Barnes, LLB., Carreiro, JE. & Degenhardt, BF. (2003) The use of osteopathic manipulative treatment as adjuvant therapy in children with recurrent acute otitis media. *Arichives in Pediatric and Adolescent Medicine* 157: 861-866.

Minde, K., Popiel, K., Leos, N. Falkner S, Parker, K. & Handley-Derry, M. (1993) The evaluation and treatment of sleep disturbances in young children. *Journal of Child Psychology and Psychiatry* 34:521-533.

Mirtz, TA., Morgan, L., Wyatt, LH. & Greene, L. (2009) An epidemiological examination of the subluxation construct using Hill's criteria of causation. *Chiropractic and Osteopathy* 2:17-13.

Moffitt, TE., Caspi, A., Dickson, N., Silva, P. & Stanton, W. (1996) Childhood-onset versus adolescent-onset antisocial conduct problems in males; natural history from age 3 to 18 years. *Developmental Psychopathology* 8:399-332.

Molfese, VJ. Rudasill, KM., Beswick, JL., Jacobi-Vessels, JL., Ferguson, MC. & White, JM. (2011) Infant Temperament, Maternal Personality, and Parenting Stress as Contributors to Infant Developmental Outcomes. *Merrill-Palmer Quarterly* 56(1):49-79.

Monson, RM., Deitz, J. & Kartin, D. (2003) The relationship between awake positioning and motor performance among infants who slept supine. *Pediatric Physical Therapy* 15:196–203.

Moore, DJ., Robb, TA. & Davidson, GP. (1988) Breath hydrogen response to milk containing lactose in colicky and non-colicky infants. *Journal of Pediatrics* 113:979-984.

Moran RW. & Gibbons, P. (2001) Intraexaminer and interexaminer reliability for palpation of the cranial rhythmic impulse at the head and sacrum. *Journal of Manipulative and Physiological Therapeutics* 24**:**183-190.

Morrell, JM. (1999) The role of maternal cognitions in infant sleep as assessed by a new instrument, the maternal cognitions about infant sleep questionnaire. *Child Psychology and Psychiatry* 40:247-258.

Morris, S., St James-Roberts, I., Sleep, J. & Gillham, P. (2001) Economic evaluation of strategies for managing crying and sleeping problems. *Archives of Disease in Childhood* 84(1):15-19.

Moss, ML. (1975) New studies of cranial growth. *Birth Defects* 11:283-295.

Moss, SD. (1997) Nonsurgical, nonorthotic treatment of occipital plagiocephaly: what is the natural history of the misshapen neonatal head? *Journal of Neurosurgery* 87:667-670.

Mower, WR. (1999) Evaluating Bias and Variability in Diagnostic Test Reports. *Annals of Emergency Medicine* 33:85-91.

Movavi Video Editor. Retrieved 26th November 2015 (www.movavi.com).

Murray, AD. Dolby, RM, Nation, RL. & Thomas, DB. (1981) Effects of epidural anaesthesia on newborns and their mothers. *Child Development* 52:71-82.

Murray, L. (1997) The effect of infants' behaviour on maternal mental health. *Health Visit* 70:334-335.

Murray, L. & Cooper, PJ. (1997) Effects of postnatal depression on infant development. *Archives of Disease in Childhood* 77(2):99-101.

Najarian, SP. (1999) lnfant cranial molding deformation and sleep position: implications for primary care. *Journal of Pediatric Health Care* 13:173-177.

Najm, WI., Seffinger, MA., Mishra, SI., Dickerson, VM., Adams, A., Reinsch, S., Murphy, LS. & Goodman, AF. (2003) Content validity of manual spinal palpatory exams - A systematic review. *BMC Complementary and Alternative Medicine* 3:1.

Nelson, AM. (2003). Transition to Motherhood. *Journal of obstetric, gynecologic, and neonatal nursing* 32(4):465-477.

Nemett, DR., Fivush, BA., Mathews, R., Camirand, N., Eldridge, MA., Finney, K. & Gerson, AC. (2008) A randomized controlled trial of the effectiveness of osteopathy-based manual physical therapy in treating pediatric dysfunctional voiding. *Journal of Pediatric Urology* 4:100-106.

Nikolopoulou, M. & St James-Roberts, I. (2003) Preventing sleeping problems in infants who are at risk of developing them. *Archives of Disease in Childhood* 88:108-111.

Nocerino, R., Pezzella, V., Cosenza, L., Amoroso, A., Di Scala, C., Amato, F., Iacono, G. & Canani, RB. (2015) The Controversial Role of Food Allergy in Infantile Colic: Evidence and Clinical Management *Nutrients* 7:2015-2025.

Nuysink, J., van Haastert, IC. Takken, T. & Helders, PJM. (2008) Symptomatic asymmetry in the first six months of life: differential diagnosis. *European Journal of Pediatrics* 167:613-619.

Oberklaid, F. (2000) Persistent crying in infancy: A persistent clinical conundrum. *Journal of Paediatric and Child Health* 36:297-298.

Oberklaid, F., Prior, M., Golvan, D., Clements, A. & Williamson, A. (1984) Temperament in Australian infants. *Australian Paediatric Journal* 20:181-184.

Oberlander, TF., Barr, RG., Young, SN. & Brian, JA. (1992) Short-term effects of feed composition on sleeping and crying in newborns. *Pediatrics* 90:733-740.

O'Connor, TG., Caprariello, P., Blackmore, ER., Gregory, AM., Glover, V. & Fleming, P. (2007) Prenatal mood disturbance predicts sleep problems in infancy and toddlerhood. *Early Human Development* 83:451-458.

O Doherty, N. (1985) *Atlas of the newborn* (2nd ed.) Lancaster, UK: MTP Press

Ohman, A., Nilsson, S., Lagerkvist, AL. & Beckung, E. (2009) Are infants with torticollis at risk of a delay in early motor milestones compared with a control group of healthy infants? *Developmental Medicine and Child Neurology* 51(7):545-550.

Olafsdottir, E., Forshei, S., Fluge, G. & Markestad, T. (2001) Randomised controlled trial of infantile colic treated with chiropractic spinal manipulation. *Archives of Disease in Childhood* 84(2):138-141.

Öhman, A. (2012) The inter-rater and intra-rater reliability of a modified "severity scale for assessment of plagiocephaly" among physical therapists. *Physiotherapy Theory and Practice* 28(5):402-406.

Ohman, A., Nilsson, S., Lagerkvist, AL. & Beckung, E. (2009): Are infants with torticollis at risk of a delay in early motor milestones compared with a control group of healthy infants? *Developmental Medicine and Child Neurology* 51(7):545-550.

Olson, SL., Bates, JE., Sandy, JM. & Schilling, EM. (2002) Early developmental precursors of impulsive and inattentive behavior: from infancy to middle childhood. Journal of Child Psychology and Psychiatry 43:435-447.

O'Mahony, F., Hofmeyr, GJ. & Menon, V. (2010) Choice of instruments for assisted vaginal delivery. *Cochrane Database of Systematic Reviews* 10(11):CD005455.

O'Neill, MB., McEvoy, MM. & Nicholson, AJ. (2014) *Diagnosing and Treating Common Problems in Paediatrics.* London UK: Radcliffe Publishing Ltd. p.96.

Orrock, P. (2009) Profile of members of the Australian osteopathic association: part 1 - the practitioners. *International Journal of Osteopathic Medicine* 12:14-24.

Overpeck, MD., Brenner, RA., Trimble, AC., Trifiletti, LB. & Brendes, HW. (1998) Risk factors for infant homicide in the United States. *New England Journal of Medicine* 339:1211–1216.

Panchal, J., Amirsheybani, H., Gurwitch, R., Cook, V., Francel, P., Neas, B. & Levine, N. (2001) Neurodevelopment in children with single-suture craniosynostosis and plagiocephaly without synostosis. *Plastic and Reconstructive Surgery* 108:1492-1498.

Papousek, M. & Papousek, H. (1990) Excessive infant crying and intuitive parental care: buffering support and its failures in parent–infant interaction. *Early Child Development and Care* 65:117-126.

Papousek, M. & von Hofacker, N. (1995) Persistent crying and parenting: Search for a butterfly in a dynamic system. *Early Development and Parenting* 4:209-224.

Papousek, M & von Hofacker, N. (1998) Persistent crying in early infancy. A non-trivial condition of risk for the developing mother-infant relationship. *Child Care Health Development* 24:395-424.

Parkin, PC., Scheartc, CJ. & Manuel, BA. (1993) Randomized controlled trial of three interventions in the management of persistent crying of infancy. *Pediatrics* 92:197-201.

Partridge, T. & Lerner, JV. (2007). A latent growth-curve approach to difficult temperament. *Infant and Child Development* 16:255-265.

Pauli-Pott, U., Becker, K., Mertesacker, T. & Beckmann, D. (2000) Infants with 'colic' – mothers' perspectives on the crying problem. *Journal of Psychosomatic Research* 48:125-132.

Pedlow, R., Sanson, A., Prior, M. & Oberklaid, F. (1993). The stability of maternally reported temperament from infancy to eight years. *Developmental Psychology* 29: 998-1007.

Pekkarinen, A., Salminen, S. & Jarvelin, MR. (2003). Hand preference and risk of injury among the Northern Finland birth cohort at the age of 30. *Laterality* 8:339-346.

Persing, JA. (2001) Discussion: Neurodevelopment in children with single-suture craniosynostosis and plagiocephaly without synostosis. *Plastic and Reconstructive Surgery* 108:1499-1500.

Persson-Blennow, I. & McNeil, TF. (1979) A questionnaire for the measurement of temperament in six-month-old infants: development and standardization. *Journal of Child Psychology and Psychiatry* 20:1-13.

Philippi, H., Faldum, A., Bergmann, H., Jung, T., Pabst, B. & Scheulpen, A. (2004) Idiopathic Infantile Asymmetry, proposal of a measurement scale. *Early Human Development* 80:79-90.

Philippi, H., Faldum, A., Jung, T., Bergmann, H., Bauer, K., Gross, D. & Spranger, J. (2006a) Patterns of postural asymmetry in infants: a standardised video-based analysis. *European Journal of Pediatrics* 165:158-164.

Philippi, H., Faldum, A., Scheulpen, A., Pabst, B., Jung, T., Bergmann, H., Bieber, I., Kaemmerer, C., Dijs, P. & Reitter, B. (2006b) Infantile postural asymmetry and osteopathic treatment: a randomized therapeutic trial. *Developmental Medicine & Child Neurology* 48:5-9.

Peitsch, WK., Keefer, CH., LaBrie, RA. & Mulliken, JB. (2002) Incidence of Cranial Asymmetry in Healthy Newborns. *Pediatrics* 110(6):e72.

Pinilla, T. & Birch, LL. (1993) Help me make it through the night: Behavioral entrainment of breast-fed infants' sleep patterns. *Pediatrics* 91:436-444.

Pizzolorusso, G., Cerritelli, F., D'Orazio, M., Cozzolino, V., Turi, P., Renzetti, C., Barlafante, G. & D'Incecco, C. (2013) Osteopathic evaluation of somatic dysfunction and craniosacral strain pattern among preterm and term newborns. *The Journal Of The American Osteopathic Association* 113 (6):462-467.

Pizzolorusso, G., Turi, P., Barlafante, G., Cerritelli, F., Renzetti, C., Cozzolino, V., D'Orazio, M., Fusilli, P., Carinci, F. & D'Incecco, C. (2011) Effect of osteopathic manipulative treatment on gastrointestinal function and length of stay of preterm infants: an exploratory study. *Chiropractic & Manual Therapies* 19(1):15.

Pollack, IF., Losken, HW. & Fasick, P. (1997) Diagnosis and Management of Posterior Plagiocephaly. *Pediatrics* 99(2):180-185.

Pogliani, L., Cerini, C., Vivaldo, T., Duca, P. & Zuccotti, GV. (2014) Deformational plagiocephaly at birth: an observational study on the role of assisted reproductive technologies. *The Journal of Maternal-Fetal & Neonatal Medicine* 27(3):270-274.

Posadzki, P., Lee, MS. & Ernst, E. (2013) Osteopathic manipulative treatment for pediatric conditions: a systematic review. *Pediatrics* 132(1):140-152.

Prechtl HFR. (1984) *Continuity and Change in Early Neural Development*. Oxford: Blackwell.

Prechtl, HFR., Einspieler, C., Cioni, G., Bos, AF., Ferrari, F. & Sontheimer, D. (1997). An early marker for neurological deficits after perinatal brain lesions. *Lancet* 349:1361-1363.

Prechtl, HFR. & Hopkins, B. (1986) Developmental transformations of spontaneous movements in early infancy. *Early Human Development* 14:233-238.

Pressler, J. L. & Hepworth, J. T. (2000). The conceptualization, measurement, and validation of transient birth trauma. *Clinical Nursing Research* 9(3):317-338.

Putnam, SP., Gartstein, MA. & Rothbart, MK. (2006). Measurement of fine-grained aspects of toddler temperament: The Early Childhood Behavior Questionnaire. *Infant Behavior & Development* 29(3):386-401.

Putnam, SP., Rothbart, MK. & Gartstein, MA. (2008). Homotypic and heterotypic continuity of fine-grained temperament during infancy, toddlerhood, and early childhood. *Infant and Child Development* 17:387-405.

Putnam, S.; Helbig, A.; Gartstein, M., Rothbart, M. & Leerkes, E. (2014) Development and Assessment of Short and Very Short Forms of the Infant Behavior Questionnaire - Revised. *Journal of Personality Assessment* 96(4):445-458.

Radesky, JS., Zuckerman, B., Silverstein, M., Rivara, FP., Barr, M., Taylor, JA., Lengua, LJ. & Barr, RG. (2013) Inconsolable Infant Crying and Maternal Postpartum Depressive Symptoms. *Pediatrics* 131(6):1857-1864.

Rahlin, M. (2005) TAMO therapy as a major component of physical therapy intervention for an infant with congenital muscular torticollis: a case report. *Pediatric Physical Therapy* 17:209-218.

Ramchandani, P., Wiggs, L., Webb, V. & Stores, G. (2000) A systematic review of treatments for settling problems and night waking in young children. *British Medical Journal* 320:209-213.

Rao, MR., Brenner, RA., Schisterman, EF., Vik, T. & Mills, JL. (2004) Long term cognitive development in children with prolonged crying. *Archives of Disease in Childhood* 89:989-992.

Rautava, P., Helenius, H. & Lehtonen, L. (1993) Psychosocial predisposing factors for infantile colic. *British Medical Journal* 307:600-604.

Rautava, P., Lehtonen, L., Helenius, H. & Sillanpaa, M. (1995) Infantile colic. Child and family characteristics three years later. *Pediatrics* 96:43-47.

Reijneveld, SA., Brugman, E. & Hirasing, RA. (2000) Infantile colic: maternal smoking as potential risk factor. *Archives of Disease in Childhood* 83:302-303.

Reijneveld, SA., Brugman, E. & Hirasing, RA.(2001) Excessive infant crying: the impact of varying definitions. *Pediatrics* 108:893-897.

Reijneveld, SA., van der Wal, MF., Brugman, E., Sing, AH. & Verloove-Vanhorick, SP. (2004). Infant crying and abuse. *Lancet* 364:1340-1342.

Rekate, HL. (1998) Occipital plagiocephaly: a critical review of the literature. *Journal of Neurosurgery* 89:24-30.

Reyna, B. & Pickler, R. (2009) Mother-infant synchrony. *Journal of Obstetric, Gynecologic, & Neonatal Nursing* 38: 470-477.

Reznick, JS., Gibbons, JL., Johnson, MO., & McDonough, PM. (1989) Behavioral inhibition in a normative sample. In J. S. Reznick (Ed.), *Perspectives on behavioral inhibition. The John D. and Catherine T. MacArthur Foundation series on mental health and development* Chicago, IL: The University of Chicago Press (pp. 25-49).

Rhoads, JM., Fatheree, NY., Norori, J., Liu, Y., Lucke, JF., Tyson, JE. & Ferris, MJ. (2009) Altered fecal microflora and increased fecal calprotectin in infants with colic. *Journal of Pediatrics* 155(6):823-828.

Righetti-Veltema, M., Conne-Perreard, E., Bousquet, A. & Manzano, J. (2002) Postpartum depression and mother-infant relationship at 3 months old. *The Journal of Affective Disorders* 70:291-306.

Robinson, S. & Proctor, M. (2009) Diagnosis and management of deformational plagiocephaly. *Journal of Neurosurgery: Pediatrics* 3:284–295.

Rogers, FJ., D'Alonzo, Jr GE., Glover, JC., Korr, IM., Osborn, GG., Patterson, MM., Seffinger, MA., Taylor, TE. & Willard, F. (2002) Proposed tenets of osteopathic medicine and principles for patient care. Journal of the American Osteopathic Association 102:63-65.

Rogers, JS. & Witt, PL. (1997) The controversy of cranial bone motion. *The Journal of orthopaedic and sports physical therapy* 26:95-103.

Ronnqvist, L. (1995) A critical examination of the Moro response in newborn infants - symmetry, state relation, underlying mechanisms. *Neuropsychologia* 33:713-726.

Rosegger, H. & Steinwendner, G. (1992) Transverse foetal position syndrome- a combination of congenital skeletal deformities in the newborn infant. *Paediatric Padol* 127:125-127.

Rothbart, MK. (1981) Measurement of temperament in infancy. *Child Development* 52:569-578.

Rothbart, MK. (1986). Longitudinal observation of infant temperament. *Developmental Psychology* 22:356-365.

Rothbart, MK., Ahadi, SA., & Hershey, KL. (1994) Temperament and social behavior in childhood. *Merrill-Palmer Quarterly* 40:21-39.

Rothbart, MK., Ahadi, SA., Hershey, .L. & Fisher, P. (2001a) Investigations of temperament at 3–7 years: The Children's Behavior Questionnaire. *Child Development* 72:1394-1408.

Rothbart, MK. & Bates, JE. (2006) Temperament. In N. Eisenberg & W. Damon (Eds.), *Handbook of child psychology: Vol. 3. Social, emotional, and personality development* (6th ed.). New York: Wiley (pp.99-166).

Rothbart, Chew, Gartstein 2001b Assessment of temperament in early development. In L.T. Singer & P.S. Zeskind (Eds.), *Biobehavioral assessment of the infant.* New York: Guilford Press (pp.190-208).

Rothbart, MK., & Derryberry, D. (1981). Development of individual differences in temperament. In M. E. Lamb & A. L. Brown (Eds.), *Advances in developmental psychology*. Hillsdale, New Jersey: Erlbaum (Vol. 1, pp.37–86).

Rothbart, M. K., & Mauro, J. A. (1990). Questionnaire approaches to the study of infant temperament. In J. W. Fagen & J. Colombo (Eds.), *Individual differences in infancy: Reliability, stability and prediction*. Hillsdale, New Jersey: Erlbaum (pp.411-429).

Rothwell, PM. (2005) RCT's have this paper External validity of randomised controlled trials: "To whom do the results of this trial apply?" *Lancet* 365:82–93.

Rowe, H. & Fisher, J. (2010) Development of a universal psycho-educational intervention to prevent common postpartum mental disorders in primiparous women: a multiple method approach *BMC Public Health* 10:499.

Rubin, SP. & Prendergast, M. (1984) Infantile colic: incidence and treatment in a Norfolk community. *Child: Care Health Development* 10:219-226.

Russell, I., Underwood, M., Brealey, S., Burton, K., Coulton, S., Farrin, A., Garratt, A., Harvey, E., Letley, L., Manca, A., Martin, J., Klaber Moffett, J., Morton, V., Torgerson, D., Vickers, M., Whyte, K. & Williams, M. (2004) United Kingdom back pain exercise and manipulation (UK BEAM) randomised trial: effectiveness of physical treatments for back pain in primary care UK BEAM Trial Team. *British Medical Journal* 19;329(7479):1377-1384.

Sackett, D. L. (2000). *Evidence-based medicine: how to practice and teach EBM*. Edinburgh: Churchill Livingstone.

Saeed, NR., Wall, SA. & Dhariwal, DK. (2008) Management of positional plagiocephaly. *Archives of Disease in Childhood* 93:82-84.

Said, G., Patois, E. & Lellouch, J. (1984) Infantile colic and parental smoking. *British Medical Journal* 289:660.

Salls, JS., Silverman, LN. & Gatty, CM. (2002) The relationship of infant sleep and play positioning to motor milestone achievement. *American Journal of Occupational Therapy* 56:577-580.

Salvesen, KÅ. & Eik-Nes, SH. (1999). Ultrasound during pregnancy and subsequent childhood non–right handedness: A meta-analysis. *Ultrasound in Obstetrics and Gynecology* 13:241-246

Sanders, G. (2003) Single system research designs in osteopathy. *Journal of Osteopathic Medicine* 6(1):19-23.

Sandhouse, ME., Shechtman, D., Sorkin, R., Drowos, JL., Caban-Martinez, AJ., Patterson, MM., Shallo-Hoffmann, J., Hardigan, P. & Snyder, A. (2010) Effect of osteopathy in the cranial field on visual function - a pilot study. *Journal of the American Osteopathic Association* 110:239-243.

Sanson, A., Prior, M., Garino, E., Oberklaid, F. & Sewell, J. (1987) The structure of infant temperament: factor analysis of the Revised Infant Temperament Questionnaire. *Infant Behavior and Development* 10:97-104.

Sanson, A., Prior, M. & Oberklaid, F. (1985) Normative data on temperament in Australian infants. *Australian Journal of Psychology* 37:185-95.

Sanson, AV., Prior, M., Oberklaid, F. & Smart, DF. (1998) Temperamental influences on psychosocial adjustment from infancy to adolescence. *The Australian Educational and Developmental Psychologist* 15:7-38.

Sanson, AV., Oberklaid, F., Pedlow, F. & Prior, M. (1991) Risk indicators: assessment of infancy predictors of pre-school behavioural maladjustment. *Journal of Child Psychology and Psychiatry* 32:609-626.

Sauber-Schatz, AK., Markovic, N., Weiss, H., Bodnar, LM., Wilson, JW. & Pearlman, MD. (2010) Descriptive epidemiology of birth trauma in the United States in 2003. *Paediatric and Perinatal Epidemiology* 24(2):116-124.

Sauls, HS. & Redfern, DE. (1997) *Colic and excessive crying*. Columbus, OH: Ross Products Division Abbott Laboratories.

Savigny, P., Kuntze, S., Watson, P., Underwood, M., Ritchie, G., Cotterell, M., Hill, D., Browne, N., Buchanan, E., Coffey, P., Dixon, P., Drummond, C., Flanagan, M., Greenough, C., Griffiths, M., Halliday-Bell, J., Hettinga, D., Vogel, S. & Walsh, D. (2009) *Low Back Pain: Early Management of Persistent non-Specific low Back Pain.* London: National Collaborating Centre for Primary Care and Royal College of General Practitioners.

Savino, F., Cordisco, L. Tarasco, V., Palumeri, E., Calabrese, R., Oggero, R., Roos, S., & Matteuzzi, D. (2010) *Lactobacillus reuteri* DSM 17938 in Infantile Colic: A Randomized, Double-Blind, Placebo-Controlled Trial. *Pediatrics* 126(3):e526-e533.

Scher, A., Zuckerman, S. & Epstein, R. (2005) Persistent night waking and settling difficulties across the first year: early precursors of later behavioural problems? *The Journal of Reproductive and Infant Psychology* 23:77-88.

Schertz, M., Zuk, L., Zin, S., Nadam, L., Schwarts, D. & Bienkowski, RS. (2008) Motor and cognitive development at one-year followup in infants with torticollis. *Early Human Development* 84:9-14.

Schmid, G., Schreier, A., Meyer, R. & Wolke, D. (2010) A prospective study on the persistence of infant crying, sleeping and feeding problems and preschool behaviour. *Acta Paediatrica* 99:286–290.

Schmitt BD. (1985) Colic: excessive crying in newborns. *Clinical Perinatology* 12:441-51.

Seffinger, MA., Najm, WI., Mishra, SI. Adams, A., Dickerson, VM., Murphy, LS. & Reinsch, S. (2004) Reliability of Spinal Palpation for Diagnosis of Back and Neck Pain. A Systematic Review of the Literature. *Spine* 29(19):e413-e425.

Senn, SJ. (2011) Francis Galton and regression to the mean. *Significance: The Royal Statistical Society* 8(3):124-126.

Sergueef, N. (2007) *Cranial Osteopathy for Infants, Children and Adolescents. A Practical Handbook.* London: Churchill Livingstone.

Sergueef, N., Nelson, KE., Glonek, T., Sergueef, N., Nelson, KE. & Glonek, T. (2006) Palpatory diagnosis of plagiocephaly. *Complementary Therapies in Clinical Practice* 12:101-110.

Sethi, S. (1995) The dialectic in becoming a mother: Experiencing a postpartum phenomenon. *Scandinavian Journal of Caring* 9:235-244.

Sherman, P., Hassall, E., Fagundes-Neto, U., Gold, BD., Kato, S., Koletzko, S., Orenstein, S., Rudolph, C., Vakil, N. & Vandeplas, Y. (2009) A global, evidence-based consensus on the definition of gastroesophageal reflux disease in the pediatric population. *American Journal of Gastroenterology* 104:1278-1295.

Siatkowski, RM., Fortney, AC., Nazir, SA., Cannon, SL., Panchal, J., Francel, P., Feuer, W. & Ahmad, W. (2005) Visual field defects in deformational posterior plagiocephaly. *Journal of Aapos: American Association for Pediatric Ophthalmology & Strabismus* 9:274-278.

Singer, JI. & Rosenberg, NM. (1992) A fatal case of colic. *Pediatric Emergency Care* 8(3):171-172.

Skjeie, H. Skonnord, T. Fetveit, A. & Brekke, M. (2013) Acupuncture for infantile colic: A blinding-validated, randomized controlled multicentre trial in general practice. *Scandinavian Journal of Primary Health Care* 31:190-196.

Sloman, J., Bellinger, DC. & Krentzel, CP. (1990) Infantile colic and transient developmental lag in the first year of life. *Child Psychiatry and Human Development* 21:25-36.

Soltis, J. (2004) The signal functions of early infant crying. *Behavioral and Brain Sciences* 27:443-490.

Sommerfeld, P., Kaidera, A. & KleinbIn, P. (2004) Inter- and intra-examiner reliability in palpation of the ‘‘primary respiratory mechanism’’ within the ‘‘cranial concept’’. *Manual Therapy* 9:22-29.

Søndergaard, C., Henriksen, TB., Obel, C. & Wisborg, K. (2001) Smoking during pregnancy and infantile colic. *Pediatrics* 108:342-346.

Søndergaard, C., Skajaa, E. & Henriksen T. (2000) Fetal growth and infantile colic. *Archives of Disease in Childhood - Fetal and Neonatal Edition* 83:f44-f47.

Sorbe, B. & Dahlgren, S. (1983) Some important factors in the molding of fetal head during vaginal delivery – a photographic study. *International Journal of Gynaecology and Obstetrics* 21(3):205-212.

Spitz, RA. (1951) *The Psychogenic Diseases in Infancy, An attempt at their etiological classification*. New York: International Universities Press (pp.255-275).

Stahlberg, M-R. (1984) Infantile colic: Occurrence and risk factors. *European Journal of Pediatrics* 143:108-111.

Stark, RE., Rose, SN. & McLagen, M. (1975) Features of infant sounds: the first eight weeks of life. *Journal of Child Language* 2:205-221.

Steiner, DI & Norman, G. (2001) *Health measurement scales: a practical guide to their development and use.* Oxford: Oxford University Press.

Stellwagen, L., Hubbard, E., Chambers, C. & Lyons Jones, K (2008) Torticollis, facial asymmetry and plagiocephaly in normal newborns. *Archives of Disease in Childhood* 93:827-831.

Stevens, B., Johnston, C., Petryshen, P. & Taddio, A. (1996) Premature infant pain profile: development and initial validation. *The Clinical Journal of Pain* 12:13-22.

Stifter, CA. & Bono, MA. (1998) The effect of infant colic on maternal self-perceptions and mother–infant attachment. *Child Care Health Development* 24:339-351.

Stifter, C. & Braungart, J. (1992) Infant colic: a transient condition with no apparent effects. *Journal of Applied Developmental Psychology* 13:447-462.

St James-Roberts, I. (1988). Persistent crying in the first year of life: a progress report. *Newsletter of the Association for Child Psychology and Psychiatry* 10:28-29.

St James-Roberts, I. (1989) Persistent crying in infancy. *Journal of Child Psychology and Psychiatry* 30:189-195.

St James-Roberts, I. (2001) Infant crying and its impact on parents. In: Barr, R.; St James-Roberts, I.; Keefe, M., editors. *New Evidence on Unexplained Early Infant Crying: Its Origins, Nature and Management.* Johnson & Johnson Pediatric Institute, NJ: Skillman, (pp.5-24).

St James-Roberts, I. (2008) Infant Crying and Sleeping: Helping Parents to Prevent and Manage Problems. *Primary Care: Clinics in Office Practice* 35(3):547-567.

St James-Roberts, I., Alvarez, M., Csipke, E., Abramsky, T., Goodwin, J. & Sorgenfrei, E. (2006) Infant crying and sleeping in London, Copenhagen and when parents adopt a "proximal" form of care. *Pediatrics*. 117(6):1146-1155.

St James-Roberts, I., Bowyer, J., Varghese, S. & Sawdon, J. (1994) Infant crying patterns in Manali and London. *Child: Care Health and Development* 20:323-337.

St. James-Roberts, I., Conroy, S. & Hurry, J. (1997) Links between infant crying and sleep-waking at six weeks of age. *Early Human Development* 48:43-52.

St James-Roberts, I., Conroy, S. & Wilsher, K. (1993) Links between maternal care and persistent infant crying in the early months. *Child: Care, Health and Development*. 24(5):353-376.

St James-Roberts, I., Conroy, S. & Wilsher, K. (1995) Clinical, developmental and social aspects of infant crying and colic. *Early Developmental Parenting* 4:177-189.

St James-Roberts I, Conroy S, Wilsher K. (1996) Bases for maternal perceptions of infant crying and colic behaviour. *Archives of Disease in Childhood* 75:375-384.

St James-Roberts, I., Conroy, S. & Wilsher, K. (1998) Links between maternal care and persistent infant crying in the early months. *Child: Care, Health and Development* 24(5):353-376.

St James-Roberts, I. & Halil, T. (1991) Infant crying patterns in the first year: normal community and clinical findings. *Journal of Child Psychology and Psychiatry* 32(6):951-968.

St James-Roberts, I., Hurry, J., Bowyer, J. & Barr, R. (1995) Supplementary carrying compared with advice to increase responsive parenting as interventions to prevent persistent infant crying. *Pediatrics* 95:381-388.

St James-Roberts, I. & Plewis, I. (1996) Individual differences, daily fluctuations, and developmental changes in amounts of infant waking, fussing, crying, feeding, and sleeping. *Child Development* 67:2527-2540.

St James-Roberts, I., Sleep, J., Morris, S., Owen, C. & Gillham, P. (2001) Use of a behavioural programme in the first 3 months to prevent infant crying and sleeping problems. *Journal of Paediatric and Child Health* 37:289-297.

St James-Roberts, I. & Wolke, D. (1988) Convergences and discrepancies among mothers' and professionals' assessments of difficult neonatal behaviour. *Journal of Child Psychology and Psychiatry* 29:21-42.

St John, D., Mulliken, JB., Kaban, LB. & Padwa, BL. (2002) Anthropometric analysis of mandibular asymmetry in infants with deformational posterior plagiocephaly. *Journal of Oral and Maxillofacial Surgery* 60:873-877.

Stone, C. (1999) *Science in the Art of Osteopathy: Osteopathic Principles and Practice.* UK: Stanley Thornes (Publishers) Ltd (p.125).

Studd, JWW., Crawford, JS., Duignan, NM., Rowbotham, CJF. & Hughes, AO. (1980) The effect of lumbar epidural analgesia on the rate of cervical dilatation and the outcome of labour of spontaneous onset. *British Journal of Obstetrics and Gynaecology* 87:1015-1021.

Sullivan, C. (1997) Introducing the cranial approach in osteopathy and the treatment of infants and mothers. *Complementary Therapies in Nursing & Midwifery* 3(3):72-76.

Sutherland, WG. (1990) *Teachings in the science of osteopathy. In: A.L. Wales [Ed.]*. Portland, Oregon: Rudra Press.

Sung, V., Hiscock, H., Tang, MLK., Mensah, FK., Nation, ML., Satzke, C., Heine, RG., Stock, A., Barr, RG. & Wake, M. (2014) Treating infant colic with the probiotic *Lactobacillus reuteri*: double blind, placebo controlled randomised Trial. *British Medical Journal* 348:2107 doi: 10.1136.

Symon, BG., Marley, JE., Martin, AJ. & Norman, ER. (2005) Effect of a consultation teaching behaviour modification on sleep performance in infants: a randomised controlled trial. *The Medical Journal of Australia* 182:215-218.

Szajewska, H., Gyrczuk, E. & Horvath, A. (2013) Lactobacillus reuteri DSM 17938 for the management of infantile colic in breastfed infants: a randomized, double-blind, placebo-controlled trial. *Journal of Pediatrics* 162(2):257-262.

Taddio, A., Nulman, I., Goldbach, M., Ipp, M. & Koren, G. (1994) Use of lidocaine-prilocaine cream for vaccination pain in infants. *Journal of Pediatrics* 124:643–648.

Tamagawa, K. & Weaver, J. (2012) Analysing adverse effects of epidural analgesia in labour. *British Journal of Midwifery* 20(10):704-708.

Taubman, B. (1984) Clinical trial of the treatment of colic by modification of parent-infant interaction. *Pediatrics* 74:998-1003.

Taubman, B. (1988) Parental counseling compared with elimination of cow's milk or soy milk protein for the treatment of infant colic syndrome: a randomized trial. *Pediatrics* 81:756-761.

Thomas, DB. (1981) Aetiological associations in infantile colic: an hypothesis. *Australian Paediatric Journal* 17:292-295.

Thomas DB. (1995) Of colic and rumbling in the guts. *Journal of Paediatrics and Child Health* 31:384-386.

Thomas, A., Birch, HG., Chess, S., Hertzig, ME. & Korn, S. (1963) *Behavioral Individuality in Early Childhood.* London: University of London Press.

Thomas, A. & Chess, S. (1977) *Temperament and Development*. New York: Brunner & Mazel.

Thomas, A., Chess, S., & Birch, HG. (1968) *Temperament and behavior disorders in children*. New York: New York University Press.

Thompson, PE., Harris, CC. & Bitowski, BE. (1986) Effects of infant colic on the family: implications for practice. *Issues in Comprehensive Pediatric Nursing* 9:273-285.

Torvaldsen, S., Roberts, CL., Simpson, JM., Thompson, JF. & Ellwood, DA. (2006) Intrapartum epidural analgesia and breastfeeding: A prospective cohort study. *International Breastfeeding Journal* 1:24.

Treem, WR. (1994) Infant colic: A pediatric gastroenterologists's perspective. *Pediatric Clinics of North America* 41:1121-1138.

Treganza, A. (1973) Explorations into posture and body mechanics. *Academic Therapy, VIII* (3):339-344.

Truecrypt (Version 7.1a). Retrieved 26th November 2015, from http://www.truecrypt.org/downloads/

Turi, P., Pizzolorusso, G. & Matteo, A. (2013) Osteopathic Manipulative Treatment During Labour: An Exploratory Study. *Archives of Disease in Childhood. Fetal and Neonatal Edition* 98(1):97.

Turk, AE., McCarthy, JG., Thorne, CH. & Wisoff, JH. (1996) The "back to sleep campaign" and deformational plagiocephaly: Is there cause for concern? *Journal of Craniofacial Surgery* 7:12-18.

Turkewitz, G. & Creighton, S. (1974) Chenges in lateral differentiation of head position in the human neonate. *Developmental Psychobiology* 8:85-89.

Underwood, M. (2009) Chiropractic and Colic. *International Journal of Clinical Practice* 63(9):1267-1274.

Van den Boom, DC. (1994) The influence of temperament and mothering on attachment and exploration: an experimental manipulation of sensitive responsiveness among lower-class mother with irritable infants. *Child Development* 6:1457-1477.

Vandenplas, Y., Badriul, H., Verghote, M., Hauser, B. & Kaufman, L. (2004) Oesophageal pH monitoring and reflux oesophagitis in irritable infants. *European Journal of Pediatrics* 163:300-304.

Vandenplas, Y., Denayer, E., Vandenbossche T, Vermet, L., Hauser, B., Deschepper, J. & Engelen, A. (2008) Osteopathy may decrease obstructive apnea in infants: a pilot study. *Osteopathic Medicine and Primary Care* 19:2-8.

Vandenplas, Y., Gottrand, F., Veereman-Wauters, G., De Greef, E., Devreker, T., Hauser, B., Benninga, M. & Heymans, HS. (2012) Gastrointestinal manifestations of cow's milk protein allergy and gastrointestinal motility. *Acta Paediatrica* 101:1105-1109.

Vandenplas, Y., Koletzko, S., Isolauri, E., Hill, D., Oranje, AP., Brueton, M., Staiano, A. & Dupont, C. (2007) Guidelines for the diagnosis and management of cow's milk protein allergy in infants. *Archives of Disease in Childhood* 92:902-908.

Vandenplas, Y., Rudolph, CD., Di Lorenzo, C., Hassall, E., Liptak, G., Mazur, L., Sondheimer, J., Staiano, A., Thomson, M., Veereman-Wauters, G. & Wenzl, TG. (2009) Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and the European Society for Pediatric Gastrenterology, Hepatology and Nutrition (ESPGHAN). *Journal of Pediatric Gastroenterology and Nutrition* 49:498-547.

Vandenplas, Y., Gutierrez-Castrellon, P., Velasco-Benitez, C., Palacios, J., Jaen, D., Ribeiro, H., Shek, LP-C., Lee, B-W. & Alarcon, P. (2013) Practical algorithms for managing common gastrointestinal symptoms in infants. *Nutrition* 29:184-194.

van der Pol, R., Smits, MJ., van Wijt, MP., Omari, T., Tabbers, M. & Benninga, M. (2011) Efficacy of proton-pump inhibitors in children with gastroesophageal reflux disease: a systematic review. *Pediatrics* 127:925-935.

van Ijzendoorn, MH. & Hubbard, FO. (2000) Are infant crying and maternal responsiveness during the first year related to infant-mother attachment at 15 months? *Attachment & Human Development* 2(3):371-391.

van Vlimmeren, LA., Helders, PJM., van Adrichem, LNA. & Engelbert, RHH. (2004) Diagnostic strategies for the evaluation of asymmetry in infancy; A review. *European Journal of Pediatrics* 163:185-191.

van Vlimmeren, LA., van der Graaf, Y., Boere-Boonekamp, MM., L'Hoir, MP., Helders, PJM. & Engelbert, RHH. (2007) Risk factors for deformational plagiocephaly at birth and at 7 weeks of age: a prospective cohort study. *Pediatrics* 119:e408-e418.

van Vlimmeren, LA., van der Graaf, Y., Boere-Boonekamp, MM, L'Hoir, MP., Helders, PJ. & Engelbert. (2008) Effect of pediatric physical therapy on deformational plagiocephaly in children with positional preference: a randomized controlled trial. *Archives of Pediatrics and Adolescent Medicine* 162:712-718.

van Wijk, RM., van Vlimmeren, LA., Groothuis-Oudshoorn, CG., Van der Ploeg, CPB., IJzerman, MJ. & Boere-Boonekamp, MM. (2014) Helmet therapy in infants with positional skull deformation: randomised controlled trial. *British Medical Journal* 348:g2741.

Vejsgaard Vestager, S., Husted-Andersen, S., Myburgh, C. & Grunnet-Nilsson, N. (2007) A possible correlation between the duration of birth and infantile colic - A short preliminary report. *Clinical Chiropractic* 10:195-197.

Ventura, N., Huguet, R., Ey, A., Montaner, A., Lizarraga, I. & Vives, E. (1998) Infantile idiopathic scoliosis in the newborn. *International Orthopaedics (SICOT)* 22:82-86.

Verhoef, MJ., Lewith, G., Ritenbaugh, C., Boon, H., Fleishman, S. & Leis, A. (2005) Complementary and alternative medicine whole systems research: Beyond identification of inadequacies of the RCT. *Complementary Therapies in Medicine* 13:206-212.

Vinkers, GJH. van Til, JA. & Boere-Boonekamp, MM. (2013) *Skull Deformation on the Treatment Preference of Youth Health Care Physicians and Paediatricians in the Netherlands Department of Health Technology and Service Research*. School of Management and Governance, University of Twente, Netherlands (pp1-21).

Vickers, A., Ohlsson, A., Lacy, JB. & Horsley, A. (2004) Massage for promoting growth and development of preterm and/or low birth-weight infants. *Cochrane Database Systematic Review* 2:CD000390.

Vik, T., Grote, V., Escribano, J., Socha, J., Verduci, E., Fritsch, M., Carlier, C., von Kries, R. & Koletzko, B. (2009) Infantile colic, prolonged crying and maternal postnatal depression. *Acta Paediatrica* 98:1344-1348.

Vles, J., van Zutphen, S., Hasaart, T., Dassen, W. & Lodder, J. (1991) Supine and prone head orientation preference in term infants. *Brain and Development* 13:87-90.

Von Heideken, J., Green, DW., Burke, SW., Sindle, K., Denneen, J., Haglund-Akerlind, Y. & Widmann, RF. (2006) The relationship between developmental dysplasia of the hip and congenital muscular torticollis. *Journal of Pediatric Orthopedics* 26(6):805-808.

Von Hofacker, N. & Papousek, M. (1998) Disorders of excessive crying, feeding and sleeping: The Munich Interdisciplinary Research and Intervention Program. *Infant Mental Health Journal* 19:180-201.

von Kries, R., Kalies, H. & Papousek, M. (2006) Excessive crying beyond 3 months may herald features of multiple regulatory problems. *Archives of Pediatrics & Adolescent Medicine* 160:508-511.

Waddell, G. (1987) A new clinical model for the treatment of low back pain. *Spine* 12**:**632-644.

Wade, S. & Kilgour, T. (2001) Extracts from ‘clinical evidence’. Infantile colic. *British Medical Journal* 323:437-440.

Wake, M., Morton-Allen, E., Poulakis, Z., Hiscock, H., Gallagher, S. & Oberklaid, F. (2006) Prevalence, stability, and outcomes of cry-fuss and sleep problems in the first 2 years of life: prospective community-based study. *Pediatrics* 117:836-842.

Walker, AM. & Menaheim, S. (1994) Intervention of supplementary carrying on normal baby crying patterns: a randomised study. *Journal of Developmental and Behavioral Pediatrics* 15:174-178

Walsh, JJ. & Morrissy, RT. (1998) Torticollis and hip dislocation. *Journal of Pediatric Orthopaedics* 18:219-221.

Weiss, H-R., Weiss, G. & Petermann, F. (2003) Incidence of curvature progression in idiopathic scoliosis patients treated with scoliosis inpatient rehabilitation (SIR): an age- and sex-matched controlled study. *Pediatric Rehabilitation* 6(1):23-30.

Weissbluth, M. (1981) Sleep duration and infant temperament. *Journal of Pediatrics* 99:817-819.

Weissbluth, M. (1987). Sleep and the colicky infant. In: C. Guilleminault (Ed.), *Sleep and Its Disorders in Children*. New York: Raven Press (pp.129-140).

Weissbluth, M., Christoffel, K. K. & Davis, T. (1984a) Treatment of infantile colic with dicyclomine hydrochloride. *Journal of Pediatrics* 104:951-955.

Weissbluth, M., Davis, AT. & Poncher, J. (1984b). Night waking in 4- to 8-month-old infants. *Journal of Pediatrics* 104:477-480.

Wessel, M., Cobb, J., Jackson, E., Harris, G. & Detwiler, A. (1954) Paroxysmal fussing in infancy, sometimes called "Colic" *Pediatrics.* 14(5):421-435.

Wescott, N. (2004) The use of cranial osteopathy in the treatment of infants with breast feeding problems or sucking dysfunction. *Australian Journal of Holistic Nursing* 11(1):25-32.

Wetherby, AM., Woods, J., Allen, L., Cleary, J., Dickinson, H. & Lord, C. (2004) Early indicators of autism spectrum disorders in the second year of life. *The Journal of Autism and Developmental Disorders* 34(5):473-493.

White, BP., Gunnar, MR., Larson, MC., Donzella, B. & Barr, RG. (2000) Behavioral and physiological responsivity, sleep, and patterns of daily cortisol production in infants with and without colic. *Child Development* 71(4):862-877.

Whiting, LM. (1911) Can the length of labour be shortened by osteopathic treatment? *Journal of the American Osteopathic Association* 11:917-921.

Wilberg, JM., Nordsteen, J. & Nilsson, N. (1999) The short-term effect of spinal manipulation in the treatment of infantile colic: a randomized controlled clinical trial with a blinded observer. *Journal of Manipulative and Physiological Therapeutics* 22(8):517-522.

Wilbrand, J-F., Seidl, M., Wilbrand, M., Streckbein, P., Bottger, S, Pons-Kuehnemann, J., Hahn, A. & Howaldt, H-P. (2013) A Prospective Randomized Trial on Preventative Methods for Positional Head Deformity: Physiotherapy versus a Positioning Pillow. *The Journal of Pediatrics* 162(6):1216-1221.

Wilkinson, J., Thomas, KJ., Freeman, JV. & McKennac, B. (2015) Day-to-day practice of osteopaths using OCF, who are affiliated with the Sutherland Cranial College of Osteopathy (SCCO): A national survey by means of a standardised data collection tool. *International Journal of Osteopathic Medicine* 18:13-21.

Williams, NH., Wilkinson, C., Russell, I., Edwards, RT., Hibbs, R. Linck, P. & Muntz, R. (2003) Randomized osteopathic manipulation study (ROMANS): pragmatic trial for spinal pain in primary care. *Family Practice* 20(6):662-669.

Winberg, J. (2005) Mother and newborn baby; mutual regulation of physiology and behaviour - a selective review. *Developmental Psychobiology* 47:217-229.

Winter, RB. (1976) Spine deformity in children: current concepts of diagnosis and treatment. *Pediatric Annals* 5:95-112.

Wolfson, A., Lacks, P. & Futterman, A. (1992) Effects of parent training on infant sleeping patterns, parents' stress, and perceived parental confidence. *Child Development* 60:41-48.

Wolke, D., Gray, P. & Meyer, R. (1994) Excessive infant crying: a controlled study of mothers helping mothers. *Pediatrics*. 94(3):322-332.

Wolke, D., Meyer, R., Ohrt, B. & Riegel, K. (1995) Co-morbidity of crying and feeding problems with sleeping problems in infancy: concurrent and predictive associations. *Early Developmental Parenting* 4:191-207.

Wolke, D., Rizzo, P. & Woods, S. (2002) Persistent infant crying and hyperactivity problems in middle childhood. *Pediatrics* 109:1054-1060.

Woods, RH. (1973) Structural normalization in infants and children with particular reference to disturbances of the central nervous system. *Journal of American Osteopathic Association* 72:903-908.

World Health Organization 2001. Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. A joint FAO/WHO expert consultation,2001.
http://www.who.int/foodsafety/publications/fs_management/probiotics/en/.
Accessed June 30, 2014.

World Health Organisation (2010). Benchmarks for Training in Osteopathy. Geneva, World Health Organization.

Worobey, J. (1986). Convergence among assessments of temperament in the first month. *Child Development* 57:47-55.

Worobey, J. (1989). Mother–infant interaction: Protocommunication in the developing dyad. In: J. F. Nussbaum (Ed.), *Life-span communication*. Hillsdale, NJ: Erlbaum (pp.7-25).

Worobey, J. (1990) In: J. Colombo & J. Fagen (Eds.), *Individual differences in infancy: Reliability, Stability, Prediction*. New Jersey: Lawrence Erlbaum Associates.

Worobey, J. (1997). Convergence between temperament ratings in infancy. *Developmental and Behavioral Pediatrics* 18:260-263.

Worobey, J. & Blajda, VM. (1989). Temperament ratings at 2 weeks, 2 months, and 1 year: Differential stability of activity and emotionality. *Developmental Psychology* 25:257-263.

Worobey, J. & Islas-Lopez, M. (2009) Temperament measures of African-American infants: change and convergence with age. *Early Child Development and Care* 179(1):107-112.

Wurmser, H., Laubereau, B., Hermann, M., Papousek, M. & von Kries, R. (2001) Excessive infant crying: often not confined to the first 3 months of age. *Early Human Development* 64:1-6.

Wyatt, K., Edwards, V., Franck, L., Britten, N., Creanor, S., Maddick, A. & Logan, S. (2011) Cranial osteopathy for children with cerebral palsy: a randomised controlled trial. *Archives of Disease in Childhood* 96:505-512.

Wynne-Davies, R. (1975) Infantile idiopathic scoliosis: causative factors, particularly in the first six months of life. *The Journal of Bone and Joint Surgery* (Br) 57:138-141.

Yu, C., Wong, F., Lo, L. & Chen, Y. (2004) Craniofacial deformity in patients with uncorrected congenital muscular torticollis: An assessment from three-dimensional computed tomography imaging. *Plastic and Reconstructive Surgery* 113:24-33.

Zentner, M., & Shiner, R. (2012) *Handbook of temperament.* New York: Guilford.

Zuzak, TJ., Boňková, J., Careddu, D., Garami, M., Hadjipanayis, A., Jazbec, J., Merrick, J., Miller, J., Ozturk, C., Persson, IA., Petrova, G., Saz Peiró, P., Schraub, S., Simões-Wüst, AP., Steinsbekk, A., Stockert, K., Stoimenova, A., Styczynski, J., Tzenova-Savova, A., Ventegodt, S., Vlieger, AM. & Längler, A. (2013) Use of complementary and alternative medicine by children in Europe: published data and expert perspectives. *Complementary Therapies in Medicine*. 21(1):s34-s47.

Chapter 16 - Appendices

Appendix 1 – Participant Information Sheet

Title of the study: The relationship between Infantile Postural Asymmetry and unsettled behaviour in babies: an observational study.

Introduction: Unsettled infant behaviour is one of the most common presentations to healthcare professionals in the first months of life. In some cases babies may be taken to osteopaths who assess tension in their muscles and movements. The aim of this study is to observe whether tension in a baby's musculoskeletal system, called Infantile Postural Asymmetry (IPA), is linked to unsettled behaviour and the research forms part of a Professional Doctorate in Osteopathy from the British School of Osteopathy (BSO) and University of Bedfordshire in the UK. This information sheet is to invite parents and guardians of babies attending the Well Baby clinics at the Rotunda Hospital, Coombe Maternity Unit and Holles Street Hospitals in Dublin to consent for their children to take part in the study. Before you decide, we would like you to understand why the research is being done and what it would involve for you and your child. Please ask us if there is anything that is not clear and we will be happy to go through it with you.

Why am I being invited to participate? You are being invited to consent to your baby participating in this study if the public health clinic that you will go to for your baby's 12 week developmental check is one of the following; Collooney Public Health Centre, Cranmore Public Health Centre or Carrick-on-Shannon Public Health Centre.

Birth and developmental stories naturally vary from baby to baby and include a wide range of characteristics that are considered normal. However, in research of this type it is important to assess babies who are similar and for this study, we are looking for babies who were born at or after 38 weeks and who are well.

Do I have to agree to my baby taking part? No, it is up to you to decide whether you wish your baby to be included in the study and whether you decide to take part, or not, will not affect your baby's health or future healthcare or your standing as a parent. If you agree to take part, you will be asked to sign a consent form but you are free to withdraw your baby from the study at any time, without giving any reasons.

<u>Your baby is eligible to join the study if:</u>

- You are attending the clinic in March 2013, when the study is taking place
- Your public health clinic is included in the list above, as this is where the 2nd stage of the study will take place at your baby's 12 week routine health check.
- Your baby was born full term (e.g. after 38 weeks gestation) and will not be receiving any medical investigations after coming to the Well-Baby clinic, as we are looking for babies with similar histories.
- Your baby has not had any physical therapy so far (e.g. osteopathy, chiropractic or physiotherapy), as this may alter study results.

What happens in the study? The study is in two parts. In the first part, you will be asked to fill out a questionnaire when your baby is 12 weeks old and this should take approximately half an hour. The questionnaire asks about your baby's behaviour in response to different activities such as hearing a noise. The questionnaire is used to assess children between 3 and 12 months, so some questions will not be relevant to your baby's stage of development and this is normal. The second part of the study will take place at your baby's 12 week developmental health check at your usual public health clinic so it will not involve extra travel or cost. Once the routine check is completed, parents will be invited to bring their babies into a separate room in the clinic where babies' movements will be videotaped for approximately 5 minutes. It is important to identify small body movements, so you will be asked to undress your baby but all identifying features such as eyes and genitalia will be blocked out on the video-tapes, so that no-one will be able to identity your baby. You will be with your baby all the time and there will be no intervention or treatment. The recording will be transferred to secure password protected computer and the images will be deleted from the camera before you leave the clinic room.

What do I have to do? If you are willing for your child to take part, you will be asked to inform the researcher (details below) and sign the consent form at the back of this pack. You have a few weeks to make this decision and can withdraw at any point. You will receive an email from the researcher a week before your baby's 12 week routine developmental health check to remind you to bring the completed consent form and questionnaire to the check up. During the video-recording session, we will give your baby an identification code and any personal information will be separated and stored securely. You will be asked to undress your baby and place him/her onto a pre-warmed sterile baby mat. There will be a cross marking on the mat and you will be shown where to position your baby on its back. The video will be started and the researcher will use distractions (such as a rattle) to encourage your baby to look right and left. You will be asked to turn your baby onto his/her tummy and the process will be repeated, which should take approx. 5 minutes and you will then dress your baby.

What are the possible benefits of taking part? There are no direct benefits to you or your child in taking part in this study but you will be contributing to research which aims to learn more about why some babies are more unsettled than others, and could lead to improved care for unsettled behaviour in babies in the future.

What are the possible disadvantages and risks of taking part? As this is an observational study, the risks are minimal. Your baby will be undressed, positioned on the mat and re-dressed by you. The researcher may help in positioning your baby on the test mat but this will be only done with your consent. Every effort will be made to keep your baby comfortable but in the unlikely event that your baby becomes upset, the session will be stopped. If your baby settles quickly and you are happy to proceed, your baby will be placed on the mat once more but you can withdraw from the study at any point, without detriment. Careful measures will be taken to protect your babies' identity. Only the researcher will have access to data and password protected software will prevent images from being accessed by unauthorised people. Personal details will be separated from questionnaires and videotapes and identities will be protected by the use of blocks over the eyes and genitalia on the recordings.

What if there is a problem? If you have any concerns or feel harmed in any way as a result of the study, please contact the researcher or one of the supervisors (contact details at the end of this sheet). The researcher is a Registered Osteopath who is covered by professional indemnity insurance and the study has been approved by the British School of Osteopathy Research Ethics Committee, the University of Bedfordshire and the AMNCH ethics committee in Dublin. If you have concerns about your baby's development, please discuss this with your child's usual healthcare practitioner.

Will my taking part in the study remain confidential? Yes, all information about your baby will be kept strictly confidential. Personal details will be separated from questionnaires and your baby will be identified by a code, not their name. The questionnaires will be scored by the main researcher and then stored securely. Recordings will moved immediately from the camera onto a password protected and encrypted file and you will be asked to watch the data being deleted from the camera before you leave. Analysis will be carried out at a later date by trained observers, who will assess each baby's position and movements on the mat. The observers will be 5 Registered Osteopaths with experience in treating and observing babies and all hold current CRB checks. When their analysis is complete, data will be stored securely, as before. At the end of the study, data will be stored securely at the British School of Osteopathy in London for a period of 6 years, after which time electronic data will be deleted and paper data will be shredded.

What will happen to the results from the study? A summary of the results will be available to all participants upon completion of the study. This is anticipated to be in the summer of 2014 and can be sent to you if you tick the box on the consent form and provide an email or postal address.

Who is organising the research: This study is being carried out by Ms. Julie Ellwood, a Registered Osteopath who works in Sligo. It is being supervised by Dr Michael Ford at the British School of Osteopathy and Professor Alf Nicholson, a Consultant Paediatrician at the National Children's Hospital in Tallaght. Thank you for taking the time to read the information sheet and our contact Information is below.

Principal Researcher

Julie Ellwood
British School of Osteopathy
275 Borough High Street
London SE1 1JE
United Kingdom
0044 (0)20 7407022
j.ellwood@bso.ac.uk

Supervisors

Professor Alf Nicholson
Paediatric Department
Children's University Hospital
Tallaght
Dublin
01 8784366
Alf.Nicholson@cuh.ie

Dr Michael Ford
British School of Osteopathy
275 Borough High Street
London SE1 1JE
UK
0044 (0) 20 70895330
m.ford@bso.ac.uk

Appendix 2 – Consent Form

CONFIDENTIAL

Participant Identification Number:

CONSENT FORM

Title of Project: The relationship between Infantile Postural Asymmetry and unsettled behaviour in babies: an observational study.

Name of Researcher: Julie Ellwood

Name of Supervisor: Dr Michael Ford and Professor Alf Nicholson

Please tick where appropriate

1.	I confirm that I have read the information sheet for the above study and have had the opportunity to ask questions	☐
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason	☐
3.	I agree to take part in the above study	☐
4.	I would like to receive a summary of the results	☐
5.	Please send a summary of the result to ……………………………………..	

Name of the Participant	Date	Signature
Researcher	Date	Signature

1 copy for the researcher: 1 copy for the participant

Appendix 3 – IBQ-Rs form

Infant Behavior Questionnaire - Revised Short form

Subject No. ________________ Date of Baby's Birth ____m ____d _____y

Today's Date ________________ Age of Child ____mos _____weeks

Sex of Child _______ Current weight_______kg Birth weight________kg

INSTRUCTIONS:

Please read carefully before starting:

As you read each description of the baby's behaviour below, please indicate how often the baby did this during the LAST WEEK (the past seven days) by circling one of the numbers in the left column. These numbers indicate how often you observed the behaviour described during the last week.

(1) Never	(2) Very Rarely	(3) Less Than Half the Time	(4) About Half the Time	(5) More Than Half the Time	(6) Almost Always	(7) Always	(X) Does Not Apply

Because this questionnaire was designed for children between 3 and 12 months, it is probable that some of the behaviours listed will not be relevant for your own baby's stage of development. It is not a cause for concern if find yourself answering 'never' to some of the questions about how your baby responds in certain situations. We are interested in how babies differ from one another in the things they do or don't do, and in how they do change as they get older but there are no right or wrong answers. If filling in this questionnaire raises any concerns about your baby's development, please feel free to discuss them with your child's usual healthcare practitioners.

The "Does Not Apply" (X) column is used when you did not see the baby in the situation described during the last week. For example, if the situation mentions the baby having to wait for food or liquids and there was no time during the last week when the baby had to wait, circle the (X) column. "Does Not Apply" is different from "Never" (1). "Never" is used when you saw the baby in the situation but the baby never engaged in the behavior listed during the last week. For example, if the baby did have to wait for food or liquids at least once but never cried loudly while waiting, circle the (1) column.

Please be sure to circle a number for <u>every</u> item.

(1) Never	(2) Very Rarely	(3) Less Than Half the Time	(4) About Half the Time	(5) More Than Half the Time	(6) Almost Always	(7) Always	(X) Does Not Apply

<u>One Week Time Span</u>

<u>How often did your baby:</u>

1 2 3 4 5 6 7 X . . . . (1) make talking sounds when s/he was ready for more food?

1 2 3 4 5 6 7 X . . . . (2) seem angry (crying and fussing) when you left her/him in the crib?

1 2 3 4 5 6 7 X . . . . (3) seem contented when left in the crib?

1 2 3 4 5 6 7 X . . . . (4) cry or fuss before going to sleep for naps?

1 2 3 4 5 6 7 X . . . . (5) look at pictures in books and/or magazines for 5 minutes or longer at a time?

1 2 3 4 5 6 7 X . . . . (6) stare at a mobile, crib bumper or picture for 5 minutes or longer?

1 2 3 4 5 6 7 X . . . . (7) play with one toy or object for 5-10 minutes?

1 2 3 4 5 6 7 X . . . . (8) play with one toy or object for 10 minutes or longer?

1 2 3 4 5 6 7 X . . . . (9) laugh aloud in play?

1 2 3 4 5 6 7 X . . . . (10) repeat the same movement with an object for minutes or longer (e.g., putting a block in a cup, kicking or hitting a mobile)?

1 2 3 4 5 6 7 X . . . . (11) smile or laugh after accomplishing something (e.g., stacking blocks, etc.)?

1 2 3 4 5 6 7 X . . . . (12) smile or laugh when given a toy?

1 2 3 4 5 6 7 X . . . . (13) enjoy being read to?

1 2 3 4 5 6 7 X . . . . (14) enjoy hearing the sound of words, as in nursery rhymes?

1 2 3 4 5 6 7 X . . . . (15) enjoy gentle rhythmic activities, such as rocking/swaying?

1 2 3 4 5 6 7 X . . . . (16) enjoy being tickled by you or someone else in your family?

1 2 3 4 5 6 7 X . . . . (17) enjoy the feel of soft blankets ?

1 2 3 4 5 6 7 X . . . . (18) enjoy being rolled up in a warm blanket?

(1) Never	(2) Very Rarely	(3) Less Than Half the Time	(4) About Half the Time	(5) More Than Half the Time	(6) Almost Always	(7) Always	(X) Does Not Apply

1 2 3 4 5 6 7 X . . . . (19) enjoy listening to a musical toy in a crib?

1 2 3 4 5 6 7 X . . . . (20) look up from playing when the telephone rang?

1 2 3 4 5 6 7 X . . . . (21) protest being placed in a confining place (infant seat, play pen, car seat, etc)?

1 2 3 4 5 6 7 X . . . . (22) startle at a sudden change in body position (for example, when moved suddenly)?

1 2 3 4 5 6 7 X . . . . (23) move quickly toward new objects?

1 2 3 4 5 6 7 X . . . . (24) show a strong desire for something s/he wanted?

1 2 3 4 5 6 7 X . . . . (25) watch adults performing household activities (e.g., cooking, etc.) for more than 5 minutes?

1 2 3 4 5 6 7 X . . . . (26) squeal or shout when excited?

1 2 3 4 5 6 7 X . . . . (27) notice low-pitched noises (e.g. air conditioner, heating system, or refrigerator running or starting up)?

1 2 3 4 5 6 7 X . . . . (28) notice a change in light when a cloud passed over the sun?

1 2 3 4 5 6 7 X . . . . (29) notice the sound of an airplane passing overhead?

1 2 3 4 5 6 7 X . . . . (30) notice a bird or a squirrel up in a tree?

1 2 3 4 5 6 7 X . . . . (31) notice fabrics with scratchy texture (e.g., wool)?

1 2 3 4 5 6 7 X . . . . (32) appear sad for no apparent reason?

<u>During feeding, how often did the baby:</u>

1 2 3 4 5 6 7 X . . . . (33) lie or sit quietly?

1 2 3 4 5 6 7 X . . . . (34) squirm or kick?

1 2 3 4 5 6 7 X . . . . (35) wave his/her arms?

(1) Never	(2) Very Rarely	(3) Less Than Half the Time	(4) About Half the Time	(5) More Than Half the Time	(6) Almost Always	(7) Always	(X) Does Not Apply

When going to sleep at night, how often did your baby:

1 2 3 4 5 6 7 X . . . . (36) fall asleep within 10 minutes?

1 2 3 4 5 6 7 X . . . . (37) have a hard time settling down to sleep?

1 2 3 4 5 6 7 X . . . . (38) settle down to sleep easily?

When being dressed or undressed during the last week, how often did the baby:

1 2 3 4 5 6 7 X . . . . (39) squirm and/or try to roll away?

1 2 3 4 5 6 7 X . . . . (40) smile or laugh?

1 2 3 4 5 6 7 X . . . . (41) coo or vocalize?

When put into the bath water, how often did the baby:

1 2 3 4 5 6 7 X . . . . (42) smile?

1 2 3 4 5 6 7 X . . . . (43) laugh?

When tossed around playfully how often did the baby:

1 2 3 4 5 6 7 X . . . . (44) smile?

1 2 3 4 5 6 7 X . . . . (45) laugh?

During a peekaboo game, how often did the baby:

1 2 3 4 5 6 7 X . . . . (46) smile?

1 2 3 4 5 6 7 X . . . . (47) laugh?

How often did your baby enjoy bouncing up and down:

1 2 3 4 5 6 7 X . . . . (48) while on your lap?

1 2 3 4 5 6 7 X . . . . (49) on an object, such as a bed, bouncer chair, or toy?

When being held, how often did the baby:

1 2 3 4 5 6 7 X . . . . (50) pull away or kick?

1 2 3 4 5 6 7 X . . . . (51) seem to enjoy him/herself?

(1) Never	(2) Very Rarely	(3) Less Than Half the Time	(4) About Half the Time	(5) More Than Half the Time	(6) Almost Always	(7) Always	(X) Does Not Apply

<u>When the baby wanted something, how often did s/he:</u>

1 2 3 4 5 6 7 X . . . . (52) become upset when s/he could not get what s/he wanted?

1 2 3 4 5 6 7 X . . . . (53) have tantrums (crying, screaming, face red, etc.) when s/he did not get what s/he wanted?

<u>When placed in an infant seat or car seat, how often did the baby:</u>

1 2 3 4 5 6 7 X . . . . (54) wave arms and kick?

1 2 3 4 5 6 7 X . . . . (55) squirm and turn body?

<u>How often did your baby make talking sounds when:</u>

1 2 3 4 5 6 7 X . . . . (56) riding in a car?

1 2 3 4 5 6 7 X . . . . (57) riding in a shopping cart?

1 2 3 4 5 6 7 X . . . . (58) you talked to her/him?

When rocked or hugged, in the last week, how often did your baby:

1 2 3 4 5 6 7 X . . . . (59) seem to enjoy her/himself?

1 2 3 4 5 6 7 X . . . . (60) seem eager to get away?

1 2 3 4 5 6 7 X . . . . (61) While being fed in your lap, how often did the baby seem eager to get away as soon as the feeding was over?

1 2 3 4 5 6 7 X . . . . (62) After sleeping, how often did the baby cry if someone didn't come within a few minutes?

1 2 3 4 5 6 7 X . . . . (63) When put down for a nap, how often did your baby settle down quickly?

1 2 3 4 5 6 7 X . . . . (64) When it was time for bed or a nap and your baby did not want to go, how often did s/he whimper or sob?

1 2 3 4 5 6 7 X . . . . (65) When face was washed, how often did the baby smile or laugh?

1 2 3 4 5 6 7 X . . . . (66) When hair was washed, how often did the baby vocalize?

1 2 3 4 5 6 7 X . . . . (67) When playing quietly with one of her/his favorite toys, how often did your baby enjoy lying in the crib for more than 5 minutes?

(1) Never	(2) Very Rarely	(3) Less Than Half the Time	(4) About Half the Time	(5) More Than Half the Time	(6) Almost Always	(7) Always	(X) Does Not Apply

1 2 3 4 5 6 7 X . . . . (68) When your baby saw a toy s/he wanted, how often did s/he get very excited about getting it?

1 2 3 4 5 6 7 X . . . . (69) When given a new toy, how often did your baby immediately go after it?

1 2 3 4 5 6 7 X . . . . (70) When placed on his/her back, how often did the baby squirm and/or turn body?

1 2 3 4 5 6 7 X . . . . (71) When frustrated with something, how often did your baby calm down within 5 minutes?

1 2 3 4 5 6 7 X . . . . (72) When your baby was upset about something, how often did s/he stay upset for up to 20 minutes or longer?

1 2 3 4 5 6 7 X . . . . (73) When being carried, how often did your baby push against you until put down?

1 2 3 4 5 6 7 X . . . . (74) When tired, how often did your baby show distress?

1 2 3 4 5 6 7 X . . . . (75) At the end of an exciting day, how often did your baby become tearful?

Two Week Time Span

When introduced to an unfamiliar adult, how often did the baby:

1 2 3 4 5 6 7 X . . . . (76) cling to a parent?

1 2 3 4 5 6 7 X . . . . (77) refuse to go to the unfamiliar person?

1 2 3 4 5 6 7 X . . . . (78) never “warm up” to the unfamiliar adult?

When you were busy with another activity and your baby was not able to get your attention, how often did s/he:

1 2 3 4 5 6 7 X . . . . (79) become sad?

1 2 3 4 5 6 7 X . . . . (80) cry?

When singing or talking to your baby, how often did s/he

1 2 3 4 5 6 7 X . . . . (81) soothe immediately?

1 2 3 4 5 6 7 X . . . . (82) take more than 10 minutes to soothe?

(1) Never	(2) Very Rarely	(3) Less Than Half the Time	(4) About Half the Time	(5) More Than Half the Time	(6) Almost Always	(7) Always	(X) Does Not Apply

<u>When showing the baby something to look at, how often did s/he:</u>

1 2 3 4 5 6 7 X . . . . (83) soothe immediately?

1 2 3 4 5 6 7 X . . . . (84) take more than 10 minutes to soothe?

<u>When patting or gently rubbing some part of the baby's body, how often did s/he:</u>

1 2 3 4 5 6 7 X . . . . (85) soothe immediately?

1 2 3 4 5 6 7 X . . . . (86) take more than 10 minutes to soothe?

1 2 3 4 5 6 7 X . . . . (87) When in the presence of several unfamiliar adults, how often did the baby continue to be upset for 10 minutes or longer?

1 2 3 4 5 6 7 X . . . . (88) When visiting a new place, how often did the baby get excited about exploring new surroundings?

1 2 3 4 5 6 7 X . . . . (89) When an unfamiliar adult came to your home or apartment, how often did your baby cry when the visitor attempted to pick her/him up?

1 2 3 4 5 6 7 X . . . . (90) When familiar relatives/friends came to visit, how often did your baby get excited?

1 2 3 4 5 6 7 X . . . . (91) When rocking your baby, how often did s/he take more than 10 minutes to soothe?

Appendix 4 – ‘Does not apply’ addition to IBQ-Rs

"*Because this questionnaire was designed for children between 3 and 12 months, it is probable that some of the behaviours listed will not be relevant for your own baby's stage of development. It is not a cause for concern if you find yourself answering ‘Never’ to some of the questions about how your baby responds in certain situations. We are interested in how babies differ from one another in the things they do or don't do, and in how they do change as they get older but there are no right or wrong answers. If filling in this questionnaire raises any concerns about your baby's development, please feel free to discuss them with your child's usual healthcare practitioners*."

“The ‘Does Not Apply’ (X) column is used when you did not see the baby in the situation described during the last week. For example, if the situation mentions the baby having to wait for food or liquids and there was no time during the last week when the baby had to wait, circle the (X) column. ‘Does Not Apply’ is different from ‘Never’ (1). ‘Never’ is used when you saw the baby in the situation but the baby never engaged in the behaviour listed during the last week. For example, if the baby did have to wait for food or liquids at least once but never cried loudly while waiting circle the (1) column.”

Appendix 5 – IBQ-Rs scoresheet

SCORING PROCEDURE

INFANT BEHAVIOR QUESTIONNAIRE - REVISED SHORT FORM

Scale scores for the Infant Behavior Questionnaire - Revised - Short From represent the mean score of all scale items applicable to the child, as judged by the caregiver. Scales' scores are to be computed by the following method:

1. Sum all numerical item responses for a given scale. Note that:

    a) If caregiver omitted an item, that item receives no numerical score;

    b) If caregiver checked the "does not apply" response option for an item, that item receives no numerical score;

    c) Items indicated with an R are reverse items and must be scored in the following way:

7 becomes 1	3 becomes 5
6 becomes 2	2 becomes 6
5 becomes 3	1 becomes 7
4 remains 4	

2. Divide the total by the number of items receiving a numerical response. Do not include items marked "does not apply (N/A)" or items receiving no response in determining the number of items.

    For example, given a sum of 47 for a scale of 12 items, with one item receiving no response, two items marked "does not apply," and 9 items receiving a numerical response, the sum of 47 would be divided by 9 to yield a mean of 5.22 for the scale score.

Note: Most statistics programs will carry out these steps for you. Users of SPSS can copy the following commands into a syntax file to reverse items and calculate scale scores. The syntax assumes that items are titled "ibq1", "ibq2", "ibq3", etc. It is also assumed that no score was entered when caregivers omitted an item or checked "Does not apply".

```
COMPUTE ibq33r = (8-ibq33).
COMPUTE ibq3r = (8-ibq3).
COMPUTE ibq82r = (8-ibq82).
COMPUTE ibq84r = (8-ibq84).
COMPUTE ibq86r = (8-ibq86).
COMPUTE ibq91r = (8-ibq91).
COMPUTE ibq37r = (8-ibq37).
COMPUTE ibq72r = (8-ibq72).
COMPUTE ibq61r = (8-ibq61).
COMPUTE ibq50r = (8-ibq50).
COMPUTE ibq60r = (8-ibq60).
COMPUTE ibq73r = (8-ibq73).

COMPUTE act = mean (ibq33r, ibq34, ibq35, ibq39, ibq54, ibq55, ibq70).
COMPUTE dist = mean (ibq2, ibq3r, ibq4, ibq21, ibq52, ibq53, ibq62).
COMPUTE fear = mean (ibq22, ibq76, ibq77, ibq78, ibq87, ibq89).
COMPUTE dura = mean (ibq5, ibq6, ibq7, ibq8, ibq10, ibq25).
COMPUTE smil = mean (ibq9, ibq11, ibq12, ibq40, ibq42, ibq43, ibq65).
COMPUTE hip = mean (ibq16, ibq44, ibq45, ibq46, ibq47, ibq48, ibq49).
COMPUTE lip = mean (ibq13, ibq14, ibq15, ibq17, ibq18, ibq19, ibq67).
COMPUTE soot = mean (ibq81, ibq82r, ibq83, ibq84r, ibq85, ibq86r, ibq91r).
COMPUTE fall = mean (ibq36, ibq37r, ibq38, ibq63, ibq71, ibq72r).
COMPUTE cudd = mean (ibq61r, ibq50r, ibq51, ibq59, ibq60r, ibq73r).
COMPUTE perc = mean (ibq20, ibq27, ibq28, ibq29, ibq30, ibq31).
COMPUTE sad = mean (ibq64, ibq74, ibq75, ibq32, ibq79, ibq80).
COMPUTE app = mean (ibq23, ibq24, ibq68, ibq69, ibq88, ibq90).
COMPUTE voc = mean (ibq1, ibq26, ibq41, ibq56, ibq57, ibq58, ibq66).
COMPUTE SUR = mean (app, voc, hip, smil, act, perc).
COMPUTE NEG = mean (sad, dist, fear, (8-fall)).
COMPUTE REG = mean (lip, cudd, dura, soot).

EXECUTE.
```

Infant Behavior Questionnaire - Revised - Short Form:

Items by Scale

I. Activity Level

Definition: Baby's gross motor activity, including movement of arms and legs, squirming, and locomotor activity.

Feeding:	During feeding, how often did the baby:
33R	lie or sit quietly?
34	squirm or kick?
35	wave arms?
Bathing and Dressing:	When being dressed or undressed during the last week, How often did the baby:
39	squirm and/or try to roll away?
Daily Activities:	When placed in an infant seat or car seat, how often did the baby:
54	wave arms and kick?
55	squirm and turn body?

When placed on his/her back, how often did the baby:

70 squirm and/or turn body?

II. Distress to Limitations

Definition: Baby's fussing, crying or showing distress while a) in a confining place or position; b) involved in caretaking activities; c) unable to perform a desired action.

How often did the baby:

2 seem angry (crying and fussing) when you left her/him in the crib?

3R seem contented when left in the crib?

4 cry or fuss before going to sleep for naps?

Daily Activities: How often during the last week did the baby:

21 protest being placed in a confining place (infant seat, play pen, car seat, etc.)?

When the baby wanted something, how often did s/he:

52 become upset when s/he could not get what s/he wanted?

53 have tantrums (crying, screaming, face red, etc.)

when s/he did not get what s/he wanted?

Sleeping: After sleeping, how often did the baby:

62 cry if someone doesn't come within a few minutes?

III. Fear

Definition: The baby's startle or distress to sudden changes in stimulation, novel physical objects or social stimuli; inhibited approach to novelty.

Daily Activities: How often during the last week did the baby:

22 startle at a sudden change in body position (e.g., when moved suddenly)?

Two Week Time Span

When introduced to an unfamiliar adult, how often did the baby:

76 cling to a parent?

77 refuse to go to the unfamiliar person?

78 never “warm up” to the unfamiliar adult?

When in the presence of several unfamiliar adults, how often did the baby:

87 continue to be upset for 10 minutes or longer?

When an unfamiliar person came to your home or apartment, how often did your baby:

89 cry when the visitor attempted to pick her/him up?

IV. Duration of Orienting

Definition: The baby's attention to and/or interaction with a single object for extended periods of time.

Play:	How often during the last week did the baby:
5	look at pictures in books and/or magazines for 5 minutes or longer at a time?
6	stare at a mobile, crib bumper or picture for 5 minutes or longer?
7	play with one toy or object for 5-10 minutes?
8	play with one toy or object for 10 minutes or longer?
10	repeat the same movement with an object for 2 minutes or longer (e.g., putting a block in a cup, kicking or hitting a mobile)?

Daily Activities:	How often during the last week did the baby:
25	watch adults performing household activities (e.g., cooking, etc.) for more than 5 minutes?

V. Smiling and Laughter

Definition: Smiling or laughter from the child in general caretaking and play situations.

Play:	How often during the last week did the baby:
9	laugh aloud in play?
11	smile or laugh after accomplishing something (e.g., stacking blocks, etc.)?
12	smile or laugh when given a toy?
Bathing/Dressing	When being dressed or undressed during the last week, how often did the baby:
40	smile or laugh?
	When put into the bath water, how often did the baby:
42	smile?
43	laugh?
	When face was washed, how often did the baby:
65	smile or laugh?

VI. High Pleasure

Definition: Amount of pleasure or enjoyment related to high stimulus intensity, rate, complexity, novelty, and incongruity.

Two Week Time Span

	How often during the last week did your baby enjoy:
16	being tickled by you or someone else in your family?
	When tossed around playfully how often did the baby:
44	smile?
45	laugh?
	During a peekaboo game, how often did the baby:
46	smile?
47	laugh?
	How often did your baby enjoy bouncing up and down:
48	while on your lap?
49	on an object, such as a bed, bouncer chair, or toy?

VII. Low Pleasure

Definition: Amount of pleasure or enjoyment related to low stimulus intensity, rate, complexity, novelty, and incongruity.

Play:	How often during the last week did the baby enjoy:
13	being read to?
14	hearing the sound of words, as in nursery rhymes?
15	gentle rhythmic activities, such as rocking or swaying?
17	the feel of soft blankets?
18	being rolled up in a warm blanket?
19	listening to a musical toy in a crib?

When playing quietly with one of her/his favorite toys, how often did your baby:

67	enjoyed lying in the crib for more than 5 minutes?

VIII. Soothability

Definition: Baby's reduction of fussing, crying, or distress when soothing techniques are used by the caretaker.

Two Week Time Span

When singing or talking to your baby, how often did s/he:

81 soothe immediately?

82R take more than 10 minutes to soothe?

When showing the baby something to look at, how often did s/he:

83 soothe immediately?

84R take more than 10 minutes to soothe?

When patting or gently rubbing some part of the baby’s body, how often did s/he:

85 soothe immediately?

86R take more than 10 minutes to soothe?

When rocking your baby, how often did s/he:

91R take more than 10 minutes to soothe?

IX. Falling Reactivity/Rate of Recovery from Distress

Definition: Rate of recovery from peak distress, excitement, or general arousal; ease of falling asleep.

Sleep: When going to bed at night, how often does your baby:

36 fall asleep within 10 minutes?

37R have a hard time settling down to sleep?

38 settle down to sleep easily?

When put down for a nap, how often did your baby:

63 settle down quickly?

Daily Activities: When frustrated with something, how often did your baby:

71 calm down within 5 minutes?

When your baby was upset about something, how often did s/he:

72R stay upset for up to 20 minutes or longer?

X. Cuddliness

Definition: The baby's expression of enjoyment and molding of the body to being held by a caregiver.

Feeding: In the last week, while being fed in your lap, how often did the baby:

61R seem eager to get away as soon as the feeding was over?

Daily Activities: When being held, how often did the baby:

50R pull away or kick?

51 seem to enjoy him/herself?

When rocked or hugged, in the last week, did your baby:

59 seem to enjoy him/herself?

60R seemed eager to get away?

When being carried, in the last week, how often did the baby:

73R push against you until put down?

XI. Perceptual Sensitivity

Definition: Amount of detection of slight, low intensity stimuli from the external environment.

Play:	How often does the infant look up from playing:
20	when the telephone rang?
	How often did your baby notice:
27	low-pitched noises (e.g., air conditioner, heating system, or refrigerator running or starting up)?
28	a change in light when a cloud passed over the sun?
29	sound of an airplane passing overhead?
30	a bird or squirrel up in a tree?
31	fabrics with scratchy texture (e.g., wool)?

XII. Sadness

New Definition: General low mood; lowered mood and activity specifically related to personal suffering, physical state, object loss, or inability to perform a desired action.

Sleeping:	When it was time for bed or a nap and your baby did not want to go, how often did s/he:
64	whimper or sob?
Daily Activities:	When tired, how often was your baby:
74	show distress?
	At the end of an exciting day, how often did your baby:
75	become tearful?
	For no apparent reason, how often did your baby:
32	appear sad?

Two Week Time Span

	When you were busy with another activity, and your baby was not able to get your attention, how often did s/he:
79	become sad?
80	cry?

XIII. Approach

Definition: Rapid approach, excitement, and positive anticipation of pleasurable activities.

Daily Activities: How often during the week did your baby:

23 move quickly toward new objects?

24 show a strong desire for something s/he wanted?

Play: When your baby saw a toy s/he wanted, how often did s/he:

68 get very excited about getting it?

When given a new toy, how often did the baby:

69 immediately go after it?

Two Week Time Span

When visiting a new place, how often did your baby:

88 get excited about exploring new surroundings?

When familiar relatives/friends visited, how often did the baby:

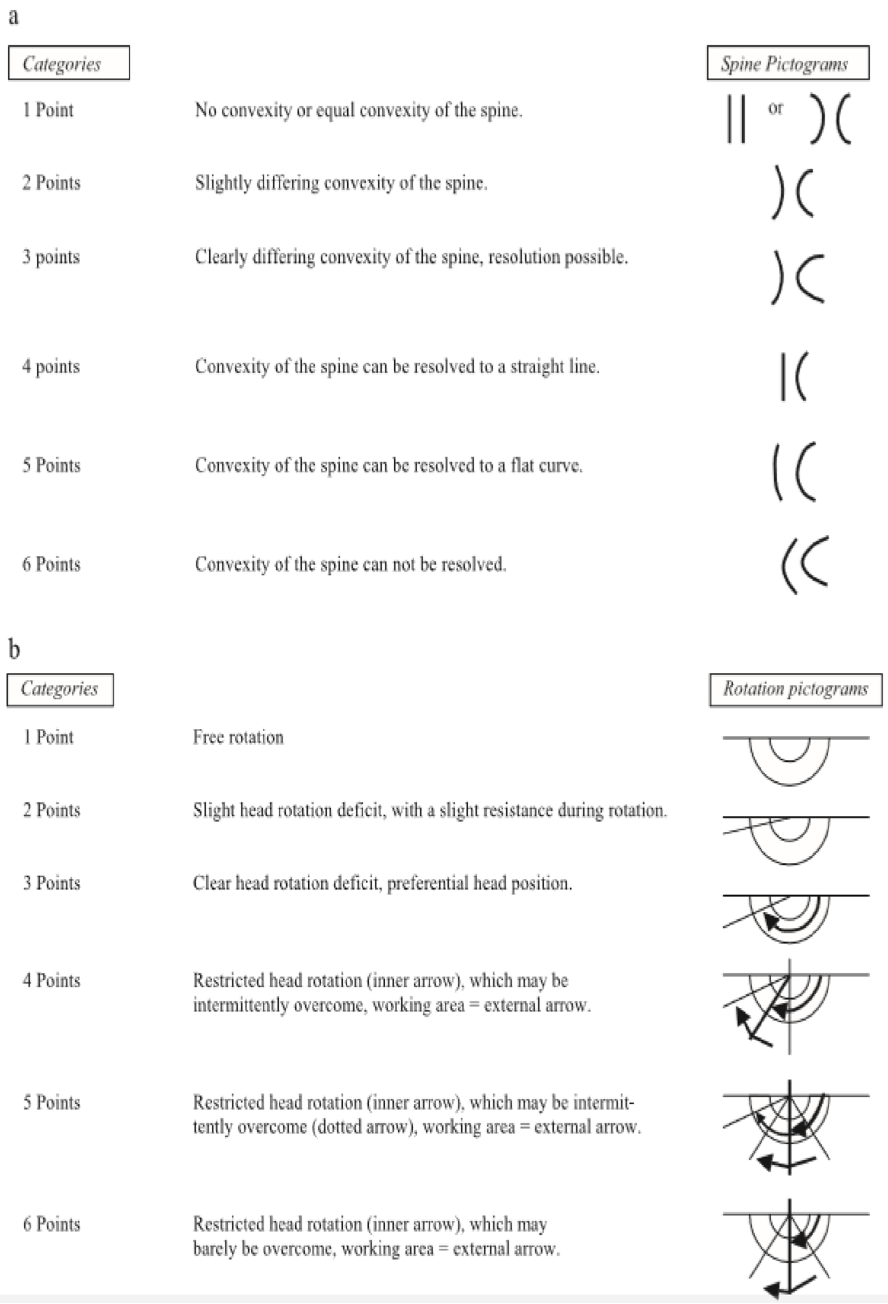
90 get excited?

XIV. Vocal Reactivity

Definition: amount of vocalization exhibited by the baby in daily activities.

Feeding:	How often did your baby make talking sounds:
1	when s/he was ready for more food?
Daily Activities:	How often during the last week did the baby:
26	squeal or shout when excited?
Bathing/Dressing	When being dressed or undressed during the last week, how often did the baby:
41	coo or vocalize?
	How often did your baby make talking sounds when:
56	riding in a car?
57	riding in a shopping cart?
58	you talked to him/her?
	When hair was washed, how often did the baby:
66	vocalize?

Appendix 6 – IPA measurement scale



a

Categories		Spine Pictograms
1 Point	No convexity or equal convexity of the spine.	or
2 Points	Slightly differing convexity of the spine.	
3 points	Clearly differing convexity of the spine, resolution possible.	
4 points	Convexity of the spine can be resolved to a straight line.	
5 Points	Convexity of the spine can be resolved to a flat curve.	
6 Points	Convexity of the spine can not be resolved.	

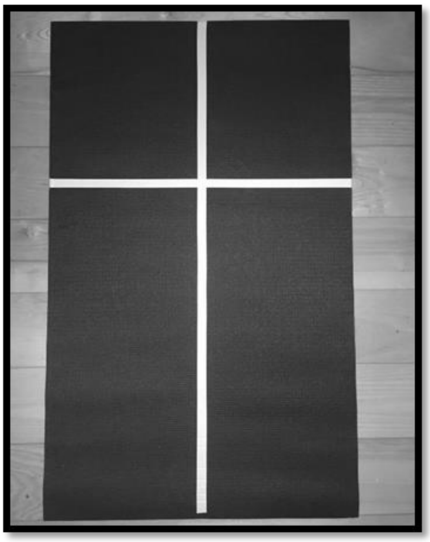
b

Categories		Rotation pictograms
1 Point	Free rotation	
2 Points	Slight head rotation deficit, with a slight resistance during rotation.	
3 Points	Clear head rotation deficit, preferential head position.	
4 Points	Restricted head rotation (inner arrow), which may be intermittently overcome, working area = external arrow.	
5 Points	Restricted head rotation (inner arrow), which may be intermittently overcome (dotted arrow), working area = external arrow.	
6 Points	Restricted head rotation (inner arrow), which may barely be overcome, working area = external arrow.	

From Philippi *et al* (2004)

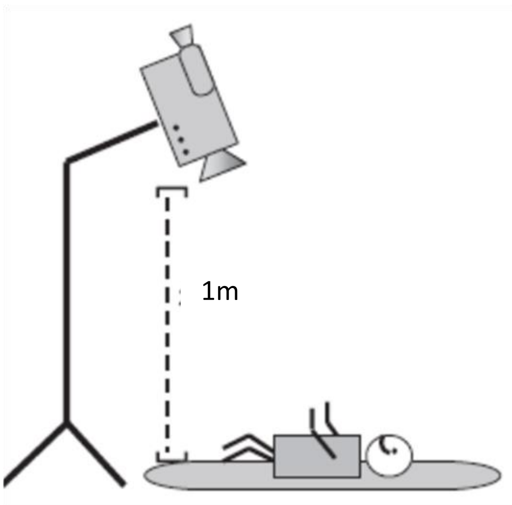
Appendix 7 – IPA test mat, camera stand and video set up

a) **IPA test mat**



b) **IPA camera stand**

c) **IPA video set up**



Appendix 8 – Patient demographics from IBQ-Rs (raw data)

Participant	DOB	Age (weeks)	Sex	Position in family	Birth Weight (kg)	Current Weight (kg)
1	07/08/2013	14	F	4	3.525	7.44
2	10/08/2013	14	M	1	3.05	5.96
3	20/07/2013	16	M	3	3.435	7.7
4	05/08/2013	14	M	3	2.71	6.02
5	15/07/2013	16	M	2	3.97	6.35
6	07/09/2013	13	M	1	3.09	7.172
7	18/09/2013	15	M	1	3.515	6.067
8	05/09/2013	13	M	3	3.742	7.711
9	03/09/2013	14	M	2	4.01	6.91
10	12/09/2013	13	F	1	3.5	6.69
11	12/09/2013	13	M	1	2.807	6.804
12	26/08/2013	15	F	3	3.345	4.139
13	28/08/2013	16	F	3	3.742	5.528
14	19/09/2013	14	M	1	3.005	5.613
15	24/09/2013	13	M	1	3.96	7.15
16	21/10/2013	13	M	4	3.884	6.549
17	24/10/2013	14	M	3	4.167	6.79
18	26/10/2013	14	M	1	3.915	6.28
19	25/10/2013	14	M	1	3.912	6.7
20	26/10/2013	14	F	4	3.005	5.35
21	17/09/2013	16	F	1	3.18	6.64
22	01/10/2013	16	F	2	4.366	5.8
23	04/11/2013	12	M	2	3.856	6.89
24	02/11/2013	15	F	1	3.45	6.54
25	07/11/2013	15	F	2	4.111	6.35
26	23/11/2013	14	M	2	3.232	6.35
27	14/11/2013	14	M	2	4	7.1
28	20/12/2013	15	M	1	3.5	6.56
29	19/12/2013	15	F	3	2.637	6.1
30	24/12/2013	14	M	2	3.856	6.6
31	19/01/2014	16	M	1	3.459	6.634
32	23/01/2014	16	M	1	3.544	6.2

Patient demographics from IBQ-Rs (raw data)						
Participant	**DOB**	**Age (weeks)**	**Sex**	**Position in family**	**Birth Weight (kg)**	**Current Weight (kg)**
33	11/03/2014	12	F	1	3.912	5.897
34	14/03/2014	14	F	3	3.374	4.082
35	21/03/2014	13	F	2	3.345	6
36	08/04/2014	15	F	1	3.572	5.925
37	10/04/2014	14	M	2	3.147	6.64
38	23/04/2014	12	F	2	3.572	5.188
39	14/04/2014	14	M	1	2.977	6.747
40	06/04/2014	14	M	3	3.827	5.897
41	13/04/2014	14	M	1	3.09	6.76
42	11/06/2014	13	M	1	3.515	7.258
43	12/07/2014	14	F	3	3.09	4.876
44	07/07/2014	14	M	2	3.6	6.719
45	04/07/2014	15	M	1	4.196	6.8
46	11/07/2014	13	F	1	3.175	6.35
47	08/07/2014	14	M	1	3.005	5.9
48	23/08/2014	15	M	2	4.252	6.45
49	27/08/2014	14	F	1	2.892	5.443
50	26/08/2014	14	F	3	3.14	6.3
51	06/10/2014	15	F	3	3.941	7.35
52	18/10/2014	13	M	3	3.884	6.56
53	08/10/2014	15	M	3	4.479	7.68
54	22/09/2014	16	M	3	2.24	6.152
55	16/10/2014	14	M	1	3.884	6.662
56	19/10/2014	14	M	3	3.459	6.946
57	15/10/2014	15	M	3	3.4	7.05
58	26/10/2014	13	M	1	3.43	6.76

Appendix 9 – IPA observer readings (raw data)

Baby ID	1 ST	1 SC	1 PT	1 PC	Total	2 ST	2 SC	2 PT	2 PC	Total	3 ST	3 SC	3 PT	3 PC	Total	Average reading 1+2+3
1	3	6	2	5	16	3	5	4	5	17	4	6	4	5	19	**17.3**
2	1	2	1	4	8	2	3	2	4	11	1	1	3	4	9	**9.3**
3	2	2	2	2	8	1	2	1	1	5	1	1	1	1	4	**5.7**
4	4	5	3	5	17	1	4	1	6	12	1	5	1	6	13	**14.0**
5	1	2	2	2	7	1	1	1	1	4	1	1	2	2	6	**5.7**
6	3	2	3	3	11	1	2	1	3	7	1	4	4	5	14	**10.7**
7	2	3	1	2	8	1	3	1	3	8	1	3	1	1	6	**7.3**
8	2	1	2	4	9	3	4	1	4	12	1	2	2	6	11	**10.7**
9	3	3	2	3	11	3	3	3	3	12	3	2	1	3	9	**10.7**
10	1	2	2	3	8	1	3	1	4	9	1	1	4	4	10	**9.0**
11	3	4	4	4	15	1	4	1	4	10	1	4	1	4	10	**11.7**
12	1	1	2	6	10	1	1	1	3	6	1	1	3	6	11	**9.0**
13	3	1	3	1	8	1	1	1	1	4	1	1	1	1	4	**5.3**
14	2	1	2	2	7	1	2	1	2	6	1	1	1	3	6	**6.3**
15	1	1	2	3	7	1	2	1	2	6	1	1	1	2	5	**6.0**
16	4	3	5	5	17	3	2	4	5	14	1	1	4	4	10	**13.7**
17	4	6	4	6	20	5	6	5	6	22	3	6	4	6	19	**20.3**
18	1	3	2	2	8	1	2	1	1	5	1	2	1	2	6	**6.3**
19	2	2	1	5	10	3	2	2	3	10	2	1	2	4	9	**9.7**
20	1	6	5	6	18	2	6	5	6	19	1	5	5	6	17	**18.0**
21	2	1	1	2	6	4	2	2	1	9	1	2	1	2	6	**7.0**
22	2	2	5	6	15	1	2	1	4	8	1	2	4	6	13	**12.0**

IPA observer readings (raw data)																
Baby ID	1 ST	1 SC	1 PT	1 PC	Total	2 ST	2 SC	2 PT	2 PC	Total	3 ST	3 SC	3 PT	3 PC	Total	**Average reading 1+2+3**
23	2	2	4	4	12	1	1	1	3	6	2	1	2	3	8	**8.7**
24	5	3	5	5	18	5	3	4	3	15	2	4	2	5	13	**15.3**
25	4	2	4	6	16	5	3	5	3	16	1	1	1	4	7	**13.0**
26	2	2	4	5	13	1	1	1	4	7	1	1	4	4	10	**10.0**
27	1	2	1	2	6	1	3	1	2	7	1	2	1	2	6	**6.3**
28	1	2	1	4	8	1	2	1	3	7	1	2	1	3	7	**7.3**
29	1	5	4	6	16	1	4	1	4	10	1	5	2	5	13	**13.0**
30	1	3	4	6	14	1	3	1	4	9	1	2	2	6	11	**11.3**
31	1	1	3	4	9	1	2	1	3	7	1	1	1	3	6	**7.3**
32	1	2	2	5	10	1	2	1	3	7	1	2	1	4	8	**8.3**
33	4	2	4	6	16	4	3	4	3	14	2	3	2	5	12	**14.0**
34	4	4	3	4	15	3	6	3	3	15	2	4	2	4	12	**14.0**
35	1	2	3	4	10	1	2	1	2	6	1	3	2	2	8	**8.0**
36	1	4	1	1	7	1	4	1	1	7	1	1	1	1	4	**6.0**
37	4	2	4	4	14	2	1	4	5	12	1	1	2	5	9	**11.7**
38	5	3	4	3	15	3	2	5	5	15	2	2	2	4	10	**13.3**
39	2	3	2	6	13	1	4	1	6	12	1	2	2	6	11	**12.0**
40	2	1	3	6	12	1	1	1	4	7	1	1	2	5	9	**9.3**
41	2	2	3	5	12	1	2	2	4	9	1	2	4	5	12	**11.0**
42	3	2	4	3	12	1	2	1	2	6	1	2	1	2	6	**8.0**
43	2	2	2	6	12	2	1	2	6	11	1	1	2	6	10	**11.0**
44	3	2	3	2	10	1	1	1	2	5	2	2	1	2	7	**7.3**

IPA observer readings (raw data)																
Baby ID	1 ST	1 SC	1 PT	1 PC	Total	2 ST	2 SC	2 PT	2 PC	Total	3 ST	3 SC	3 PT	3 PC	Total	**Average reading 1+2+3**
45	1	3	2	4	10	1	1	2	4	8	1	2	2	4	9	**9.0**
46	2	2	3	3	10	1	2	1	4	8	1	2	5	5	13	**10.3**
47	2	1	2	2	7	1	2	1	3	7	1	2	1	4	8	**7.3**
48	3	3	2	5	13	1	1	1	3	6	1	2	1	4	8	**9.0**
49	2	1	3	5	11	1	2	1	4	8	1	1	4	5	11	**10.0**
50	1	1	1	3	6	1	1	1	3	6	1	1	1	3	6	**6.0**
51	1	1	2	4	8	1	2	1	4	8	2	2	2	5	11	**9.0**
52	1	1	1	1	4	1	1	1	1	4	1	2	1	3	7	**5.0**
53	3	2	2	6	13	3	3	4	6	16	2	3	5	6	16	**15.0**
54	1	6	1	4	12	1	1	1	1	4	1	2	2	3	8	**8.0**
55	1	5	2	3	11	1	4	1	4	10	1	5	1	4	11	**10.7**
56	4	3	1	3	11	2	3	1	4	10	1	3	2	4	10	**10.3**
57	1	2	4	6	13	1	2	4	6	13	2	2	2	6	12	**12.7**
58	3	3	3	3	12	1	2	4	4	11	2	3	1	4	10	**11.0**

Appendix 10 – IBQ-Rs subsets (raw data)

Baby ID	act	dist	fear	dura	smil	hip	lip	soot	fall	cudd	perc	sad	app	voc
1	3.14	5.29	1.5	5.4	5	6.14	5	6.71	5	6.67	4.8	4.67	4.17	4.57
2	3.14	3.14	1.83	4.8	3.71	4.86	5.29	6.71	6.67	5.83	4.6	1.5	4.25	4.67
3	2.14	2.57	1.83	2.75	5.5	4.8	5.17	6.43	5.83	6.5	3	3	4	5.57
4	3.14	2.86	1.6	4.67	4.67	6	5.29	7	5.83	6.17	5.8	1.5	4	5.17
5	3.86	2.71	2.33	5.5	5.33	5.86	6.29	6.43	6.17	6.8	5.25	2	5.83	5.43
6	5.5	5.43	4.67	2.8	6.5	6.67	7	4.14	4.5	4.4	6	5.8	5.67	5.71
7	2.17	3	2	3.5	3	4.86	4.4	5.71	6	6.75	1	2.4	4	4
8	3.14	3.5	3.83	4.5	3.83	5.14	4.8	3.71	5	6.17	4	4.6	3.5	3
9	3.29	5	2.25	6	3.43	5	6	6.29	6.33	6.67	2.33	4.67	5.17	3.33
10	4.6	5.57	4	4.6	3.71	6	3.75	6.17	6.25	4	7		7	6.4
11	2	3.29	1.67	5.67	4	5.75	6.5	6.57	6.5	6	3.67	4.33	4.25	3.43
12	3	3.6	1.83	3.83	4.5	6	5.17	6	4.67	4.6	3.75	3.8	3.75	4.75
13	3.86	3.8	6	5	4.6	3.8	6	4.14	6.17	6.4	2.5	5.75		4
14	3.86	3.29	2	3.67	3.17	3.14	5.5	5.29	4.67	5.83	2	4.6	5	4
15	4.33	3.4	1.67	4	5.71	4.71	3.29	5.29	4	6.33	2	4.17	5	3.67
16	1.71	1.43	1.5	3.5	3.86	6	5.43	7	6.67	6	1.67	1.5	3.5	3.29
17	4.57	5.14	2.67	3.33	5	3.71	4.86	4.14	4.67	5.33	4.25	5	4.6	5.86
18	3.14	4.57	2	3.83	4.29	3.57	3.71	4.57	4.67	6.5	4.25	5	3.5	4.29
19	4.43	3.29	1.5	1.2	3.33	4	4.14	3.57	5.33	6.17	2.5	4.5	3.17	3.86
20	3	3.5	3	3.25	2.4	3	5	5.71	5.17	5.2	1	3.67	1.5	3
21	3.43	4.43	1.83	6	6.67	6.57	7	6.57	4.8	6.17	6.33	4.25	5.67	6
22	3	3.29	1.67	4.17	2.29	5.43	5	6.14	6.5	6.5	3.67	3.67	2	4.86
23	2.43	4.29	1.83	3.83	3.5	3.2	4	3.43	5.17	4.67	4.67	5	2.83	2.71
24	3.29	3.43	2.67	4.33	5.25	4.33	4.43	6.57	6.17	6	4	4	4.75	4.71
25	3.29	2.5	6.17	6	3.67	5.14	6.33	7	6.83	6.6	4.33	4	4.83	6.14
26	4.29	2.71	2.17	3.4	5	6.33	6.29	5.43	5.33	6.67	4	4.83	5.2	5
27	4.57	3	1.17	5.17	3.57	5.14	4	6.14	6	5.5	4.6	3.33	5.33	3.43
28	1.14	3.29	1	2.8	3.43	5.71	4.29	6.14	5.17	7	1	2.67	3.4	3.86
29	4.14	3.71	3.33	4.2	3.33	2.17	5.29	2.71	4.67	4.67	4.5	5.4	2.75	3.57
30	2.14	3.5	1.67	3.2	4.5	3.4	5.5	6.57	5.67	4.17	2.33	3.5	4.67	4.29
31	3	2.2	1.83	3.33	4.14	4	5.6	5.14	6.6	6.2	1.83	2.83	2	4.5
32	3.57	3.14	2	5.17	5.33	4.86	5.71	5.43	6.33	6	5.5	2	5.4	4.67
33	4.29	3.86	2.17	3.17	3.57	3.71	5.43	4.86	6	6.33	2.33	2.33	3.5	5.29
34	4	3.14	4	6.5	3.5	6	6	5.43	6.17	5.33	5.75	3.8	6	4.14
35	2.57	4.71	1	4	4.17	5	5.43	5.43	6	6.33	3.6	3.33	3.33	3.57
36	4.57	3.57	2.33	5.5	4.43	5	5.29	4.43	3	3.17	4	6.2	5.33	3.14
37	2.29	3.5	1.5	3.8	5.5	6.33	6.43	6.57	6.33	6.83	6.25	3.4	5	5.33
38	2.29	4.14	2.5	3.6	4.8	5.5	5.86	5.67	6.5	7	5.75	1.83	4.5	5.33
39	4.4	5	2.33	4.2	3.83	4.71	5.14	4.43	4.67	6	4.67	4.17	5	5
40	3	3.29	3.5	3	6.71	6.14	5.86	7	6.5	7	3.67	2.67	3.33	5.29
41	2.43	2	1.67	4.8	5.33	7	5	6.43	6	6.67	6.33	2.5	6	5.2
42	2.43	2.5	1.67	3.4	5.5	5.29	5.17	3.86	5.17	6.83	6	3	4.5	5.67

IBQ-Rs subsets (raw data)														
Baby ID	**act**	**dist**	**fear**	**dura**	**smil**	**hip**	**lip**	**soot**	**fall**	**cudd**	**perc**	**sad**	**app**	**voc**
43	5	5.14	2	4.33	3.83	3.2	4.6	4.17	3.5	6	5.5	6.2	2.25	3.33
44	3.43	1.43	1.83	2.83	4.14	3.86	3.57	6.43	6.83	6.83	1.67	1.5	1.67	3.57
45	3.71	4.5	2.17	6	5.17	2	6.8	6	6	6.5	3	4.33	6.75	5
46	3.29	4.57	2.83	3.33	5.43	6.86	6	6.43	6.17	6.5	3.67	4.33	6	5.43
47	3	2.67	2.67	2.33	4.29	4.8	4.5	5.4	4	6	5.67	1.67	1.5	6
48	2.43	2.33	1.5	5.83	5.83	4.5	4.71	6.2	4.67	4.67	4.2	3.17	4.5	6.17
49	3.29	3	2.17	6	4.83	3.83	5.5	6.43	5.5	5.83	4.33	2.5	5.2	4.29
50	6	5.57	1.33	3.67	3.5	4.17	6.43	5.43	3.33	6.5	3.8	4.5	4.17	4.43
51	4.25	2.67	1.6	7	6.17	6.43	6.75	6.14	6.25	7	7	2.25	6	6.33
52	3.17	4.43	2.33	4.4	3.67	5	4.57	4.86	3.67	5.5	5	3.5	4.25	4
53	3.71	4	2.5	7	4.14	6.71	6.2	6.43	6.83	3.33	4	2.67	4.8	4.5
54	2.83	2.2	2	4.8	4	5.5	7	7	6.6	7	1	1.33	5	4
55	2	3.8	6	5.4	4.67	5	3.8	5.8	4.83	5.33	3	3.33	5	3.57
56	3	3.8	1.33	5.2	6	5.29	5.14	5.29	5.67	5.5	5	3.83	5	6
57	3.57	4.29	1.6	3.6	2.57	3.83	6	5.57	3.17	7	2.33	4.5	1.75	3.33
58	2.57	5	1.83	3.83	3.67	4.4	5	3.57	5.17	6	2.8	4	2.5	3.17

Appendix 11 – IBQ-Rs broad scales (raw data)

Baby ID	SUR	NEG	REG
1	4.64	3.61	5.95
2	4.21	1.95	5.66
3	4.17	2.39	5.21
4	4.8	2.03	5.78
5	5.26	2.22	6.25
6	6.01	4.85	4.59
7	3.17	2.35	5.09
8	3.77	3.73	4.8
9	3.76	3.4	6.24
10	5.79	3.77	4.63
11	3.85	2.7	6.18
12	4.29	3.14	4.9
13	3.75	4.35	5.39
14	3.53	3.3	5.07
15	4.24	3.31	4.73
16	3.34	1.44	5.48
17	4.67	4.04	4.42
18	3.84	3.73	4.65
19	3.55	2.99	3.77
20	2.32	3.25	4.79
21	5.78	3.43	6.43
22	3.54	2.53	5.45
23	3.22	3.49	3.98
24	4.39	2.98	5.33
25	4.57	3.46	6.48
26	4.97	3.1	5.45
27	4.44	2.38	5.2
28	3.09	2.45	5.06
29	3.41	3.95	4.22
30	3.55	2.75	4.86
31	3.25	2.07	5.07
32	4.89	2.2	5.58
33	3.78	2.59	4.95
34	4.9	3.19	5.82
35	3.71	2.76	5.3
36	4.41	4.28	4.6
37	5.12	2.52	5.91
38	4.69	2.49	5.53
39	4.6	3.71	4.94
40	4.69	2.74	5.71
41	5.38	2.04	5.72
42	4.9	2.5	4.81

IBQ-Rs broad scales (raw data)			
Baby ID	**SUR**	**NEG**	**REG**
43	3.85	4.46	4.78
44	3.06	1.48	4.92
45	4.27	3.25	6.33
46	5.11	3.39	5.57
47	4.21	2.75	4.56
48	4.6	2.58	5.35
49	4.3	2.54	5.94
50	4.34	4.02	5.51
51	6.03	2.07	6.72
52	4.18	3.65	4.83
53	4.65	2.58	5.74
54	3.72	1.73	6.45
55	3.87	4.08	5.08
56	5.05	2.82	5.28
57	2.9	3.8	5.54
58	3.18	3.42	4.6